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(54) Polymorphisms associated with hypertension

(57) The invention discloses a collection of polymorphic sites in genes know or suspected to have a role in hypertension. The invention provides nucleic acids including such polymorphic sites. The nucleic acids can be used as probes or primers or for expressing variant proteins. The invention also provide methods of analyzing the polymorphic forms occupying the polymorphic sites.

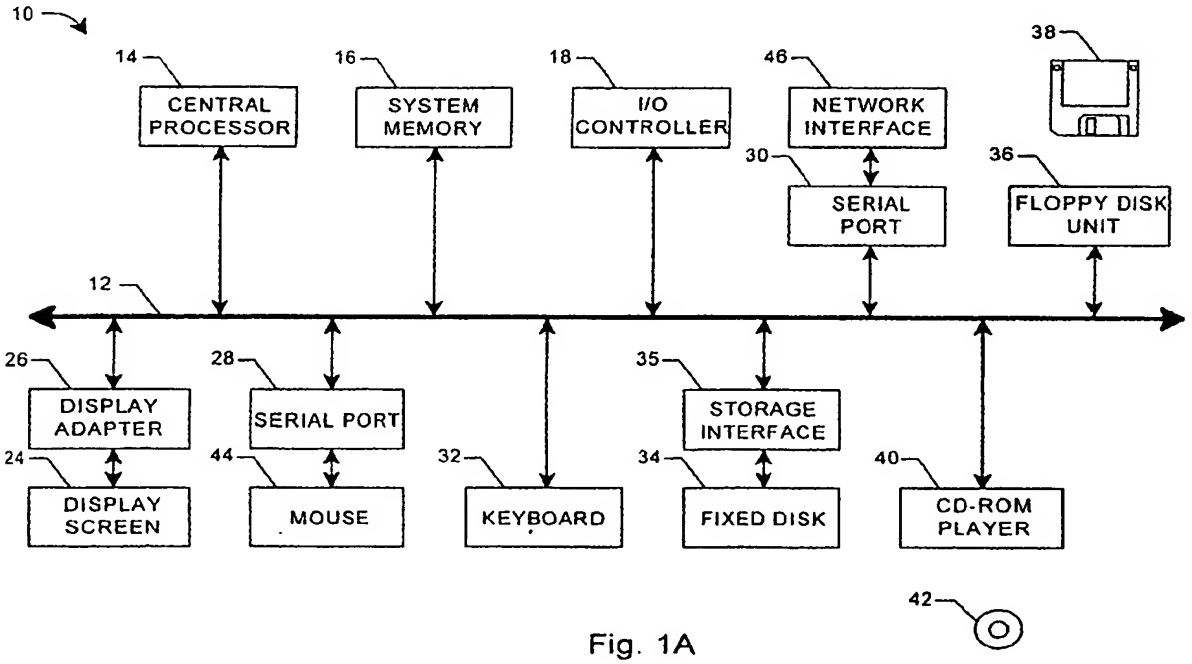

Fig. 1A

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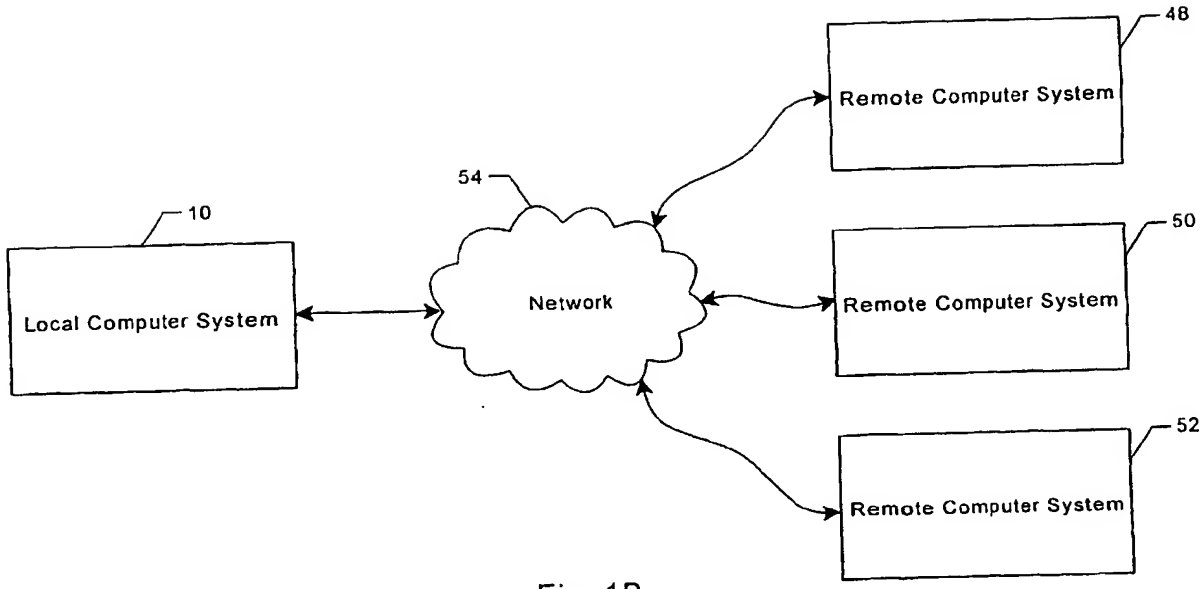


Fig. 1B

Description

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] This application derives priority from USSN 60/084,641 filed May 7, 1998, which is incorporated by reference in its entirety for all purposes.

[0002] The work described in this application was funded, in part, by a grant from the National Heart, Lung & Blood Institute (U10 HL54466), which may have certain rights in this invention.

BACKGROUND OF THE INVENTION

[0003] Hypertension, or high blood pressure, is a common disease affecting 50 million Americans and contributing to over 200,000 deaths annually from stroke, myocardial infarction, and end-stage renal disease. The disease is multifactorial and numerous genetic and nongenetic components, such as salt intake, age, diet, and body mass, are suspected to contribute. A specific cause of hypertension can typically be identified in only a small percentage of patients. Other patients with abnormally high blood pressure of unknown cause are said to have essential hypertension.

[0004] The existence of a genetic component to hypertension is known from twin studies, which have revealed a greater concordance of blood pressure in monozygotic twins that in dizygotic twins. Similarly, biological siblings have show greater concordance of blood pressure than adoptive siblings raised in the same household. Such studies have suggested that up to about 40% of the variations in blood pressure in the population are genetically determined.

[0005] There is a substantial pool of candidate genes that may contribute to the genetic component of hypertension. Because blood pressure is determined by the product of cardiac output and vascular resistance, candidate genes may act through either pathway. Physiologic pathways which are know to influence these parameters include the renin-angiotensin-aldosterone system, which contributes to determination of both cardiac output and vascular resistance. In this pathway, angiotensinogen, a hormone produced in the liver, is cleaved by an enzyme called renin to angiotensin I, which then undergoes further cleavage by angiotensin I-converting enzyme (ACE) to produce the active hormone angiotensin II (AII). AII acts through specific AT1 receptors present on vascular and adrenal cells. Receptors present on vascular cells cause vasoconstriction of blood vessels. Receptors present on adrenal cells cause release of the hormone aldosterone by the adrenal gland. This hormone acts on the mineralocorticoid receptor to cause increase sodium reabsorption largely through a renal epithelial sodium location. Other candidate genes are those of peripheral and central adrenergic pathways, which have dominant effects on cardiac iontropy, heart rate and vascular resistance; a variety of renal ion channels and transporters, which determine net sodium absorption and hence intravascular volume; calcium channels and exchangers and nitric oxide pathways, whose activity influences vascular tone. Another candidate gene encodes atrial natriuretic factor precursor, which is cleaved to atrial natriuretic peptides, found in the heart atrium, an endocrine organ controlling blood pressure and organ volume.

[0006] For some of the above candidate genes, variant forms have been identified that occur with increased frequency in individuals with hypertension. For example, a number of the polymorphisms have been reported in the angiotensinogen gene (AGT). In one of these, an M/T substitution at position 235, the T allele occurs more frequently in individuals with hypertension suggesting that this polymorphic form is a cause of hypertension or in equilibrium dislinkage with another polymorphism that is a cause. Jeunmaitre et al., Am. J. Hum. Genet. 60, 1448-1460 (1997). Two other genes within the renin-angiotensin-aldosterone system also have variant forms correlated with specific forms of hypertension, that is, aldosterone synthase gene and the gene encoding the β-subunit of the epithelial sodium channel induced by the mineralocorticoid receptor. Lifton et al., Proc. Natl. Acad. Sci. USA 92, 8548-8551 (1995).

[0007] Despite these developments, only a minute proportion of the total repository of polymorphisms in candidate genes for hypertension has been identified, and the primary genetic determinants of hypertension remain unknown in most affected subjects, as does the nature of the interaction between different genetic determinants. The paucity of polymorphisms hitherto identified is due to the large amount of work required for their detection by conventional methods. For example, a conventional approach to identifying polymorphisms might be to sequence the same stretch of oligonucleotides in a population of individuals by dideoxy sequencing. In this type of approach, the amount of work increases in proportion to both the length of sequence and the number of individuals in a population and becomes impractical for large stretches of DNA or large numbers of persons.

SUMMARY OF THE INVENTION

[0008] The invention provides nucleic acids of between 10 and 100 bases comprising at least 10 contiguous nucleotides including a polymorphic site from a sequence shown in Table 1, column 8 or the complement thereof. The nucleic acids can be DNA or RNA. Some nucleic acids are between 10 and 50 bases and some are between 20 and 50 bases. The base occupying the polymorphic site in such nucleic acids can be either a reference base shown in Table 1, column

3 or an alternative base shown in Table 1, column 5. In the some nucleic acids, the polymorphic site is occupied by a base that correlates with hypertension or susceptibility thereto. Some nucleic acids contain a polymorphic site having two polymorphic forms giving rise two different amino acids specified by the two codons in which the polymorphic site occurs in the two polymorphic forms.

[0009] The invention further provides allele-specific oligonucleotides that hybridize to a nucleic acid segment shown in Table 1, column 8 or its complement, including the polymorphic site. Such oligonucleotides are useful as probes or primers.

[0010] The invention further provides methods of analyzing a nucleic acid sequence. Such methods entail obtaining the nucleic acid from an individual; and determining a base occupying any one of the polymorphic sites shown in Table 1 or other polymorphic sites in equilibrium dislinkage therewith. Some methods determine a set of bases occupying a set of the polymorphic sites shown in Table 1. In some methods, the nucleic acid is obtained from a plurality of individuals, and a base occupying one of the polymorphic positions is determined in each of the individuals. Each individual is then tested for the presence of a disease phenotype, and correlating the presence of the disease phenotype with the base, particularly hypertension.

[0011] In another aspect, the invention provides nucleic acids comprising an isolated nucleic acid sequence of Table 1, column 8 or the complement thereof, wherein the polymorphic site within the sequence or its complement is occupied by a base other than the reference base show in Table 1, column 3. Such nucleic acids are useful, for example, in expression of variant proteins or production of transgenic animals.

[0012] The invention further provides methods of diagnosing a phenotype. Such methods entail determining which polymorphic form(s) are present in a sample from a subject at one or more polymorphic sites shown in Table 1, and diagnosing the presence of a phenotype correlated with the form(s) in the subject.

[0013] The invention also provides methods of screening polymorphic sites linked to polymorphic sites shown in Table 1 for suitability for diagnosing a phenotype. Such methods entail identifying a polymorphic site linked to a polymorphic site shown in Table 1, wherein a polymorphic form of the polymorphic site shown in Table 1 has been correlated with a phenotype. One then determines haplotypes in a population of individuals to indicate whether the linked polymorphic site has a polymorphic form in equlibrium dislinkage with the polymorphic form correlated with the phenotype.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] Figs. 1A and 1B depict computer systems suitable for storing and transmitting information relating to the polymorphisms of the invention.

DEFINITIONS

[0015] A nucleic acid can be DNA or RNA, and single- or double-stranded. Oligonucleotides can be naturally occurring or synthetic, but are typically prepared by synthetic means. Preferred nucliec acids of the invention include segments of DNA, or their complements including any one of the polymorphic sites shown in Table 1. The segments are usually between 5 and 100 contiguous bases, and often range from 5, 10, 12, 15, 20, or 25 nucleotides to 10, 15, 30, 25, 20, 50 or 100 nucleotides. Nucleic acids between 5-10, 5-20, 10-20, 12-30, 15-30, 10-50, 20-50 or 20-100 bases are common. The polymorphic site can occur within any position of the segment. The segments can be from any of the allelic forms of DNA shown in Table 1. For brevity in Table 1, the symbol T is used to represent both thymidine in DNA and uracil in RNA. Thus, in RNA oligonucleotides, the symbol T should be construed to indicate a uracil residue.

[0016] Hybridization probes are capable of binding in a base-specific manner to a complementary strand of nucleic acid. Such probes include nucleic acids, peptide nucleic acids, as described in Nielsen et al., Science 254, 1497-1500 (1991).

[0017] The term primer refers to a single-stranded oligonucleotide capable of acting as a point of initiation of template-directed DNA synthesis under appropriate conditions (i.e., in the presence of four different nucleoside triphosphates and an agent for polymerization, such as, DNA or RNA polymerase or reverse transcriptase) in an appropriate buffer and at a suitable temperature. The appropriate length of a primer depends on the intended use of the primer but typically ranges from 15 to 30 nucleotides. Short primer molecules generally require cooler temperatures to form sufficiently stable hybrid complexes with the template. A primer need not reflect the exact sequence of the template but must be sufficiently complementary to hybridize with a template. The term primer site refers to the area of the target DNA to which a primer hybridizes. The term primer pair means a set of primers including a 5' upstream primer that hybridizes with the 5' end of the DNA sequence to be amplified and a 3', downstream primer that hybridizes with the complement of the 3' end of the sequence to be amplified.

[0018] Linkage describes the tendency of genes, alleles, loci or genetic markers to be inherited together as a result of their location on the same chromosome, and can be measured by percent recombination between the two genes, alleles, loci or genetic markers. Loci occurring within 50 centimorgan of each other are linked. Some linked markers

occur within the same gene or gene cluster.

[0019] Polymorphism refers to the occurrence of two or more genetically determined alternative sequences or alleles in a population. A polymorphic marker or site is the locus at which divergence occurs. Preferred markers have at least two alleles, each occurring at frequency of greater than 1%, and more preferably greater than 10% or 20% of a selected population. A polymorphic locus may be as small as one base pair. Polymorphic markers include restriction fragment length polymorphisms, variable number of tandem repeats (VNTR's), hypervariable regions, minisatellites, dinucleotide repeats, trinucleotide repeats, tetranucleotide repeats, simple sequence repeats, and insertion elements such as Alu. The first identified allelic form is arbitrarily designated as a the reference form and other allelic forms are designated as alternative or variant alleles. The allelic form occurring most frequently in a selected population is sometimes referred to as the wildtype form. Diploid organisms may be homozygous or heterozygous for allelic forms. A diallelic polymorphism has two forms. A triallelic polymorphism has three forms.

[0020] A single nucleotide polymorphism occurs at a polymorphic site occupied by a single nucleotide, which is the site of variation between allelic sequences. The site is usually preceded by and followed by highly conserved sequences of the allele (e.g., sequences that vary in less than 1/100 or 1/1000 members of the populations).

[0021] A single nucleotide polymorphism usually arises due to substitution of one nucleotide for another at the polymorphic site. A transition is the replacement of one purine by another purine or one pyrimidine by another pyrimidine. A transversion is the replacement of a purine by a pyrimidine or vice versa. Single nucleotide polymorphisms can also arise from a deletion of a nucleotide or an insertion of a nucleotide relative to a reference allele.

[0022] A set of polymorphisms means at least 2, and sometimes 5, 10, 20, 50 or more of the polymorphisms shown in Table 1.

[0023] Hybridizations are usually performed under stringent conditions, for example, at a salt concentration of no more than 1 M and a temperature of at least 25□C. For example, conditions of 5X SSPE (750 mM NaCl, 50 mM Na Phosphate, 5 mM EDTA, pH 7.4) and a temperature of 25-30□C are suitable for allele-specific probe hybridizations.

[0024] An isolated nucleic acid means an object species invention that is the predominant species present (i.e., on a molar basis it is more abundant than any other individual species in the composition). Preferably, an isolated nucleic acid comprises at least about 50, 80 or 90 percent (on a molar basis) of all macromolecular species present. Most preferably, the object species is purified to essential homogeneity (contaminant species cannot be detected in the composition by conventional detection methods).

[0025] Linkage disequilibrium or allelic association means the preferential association of a particular allele or genetic marker with a specific allele, or genetic marker at a nearby chromosomal location more frequently than expected by chance for any particular allele frequency in the population. For example, if locus X has alleles a and b, which occur equally frequently, and linked locus Y has alleles c and d, which occur equally frequently, one would expect the haplotype ac to occur with a frequency of 0.25 in a population of individuals. If ac occurs more frequently, then alleles a and c are in linkage disequilibrium. Linkage disequilibrium may result from natural selection of certain combination of alleles or because an allele has been introduced into a population too recently to have reached equilibrium with linked alleles.

[0026] A marker in linkage disequilibrium can be particularly useful in detecting susceptibility to disease (or other phenotype) notwithstanding that the marker does not cause the disease. For example, a marker (X) that is not itself a causative element of a disease, but which is in linkage disequilibrium with a gene (including regulatory sequences) (Y) that is a causative element of a phenotype, can be used detected to indicate susceptibility to the disease in circumstances in which the gene Y may not have been identified or may not be readily detectable. Younger alleles (i.e., those arising from mutation relatively late in evolution) are expected to have a larger genomic sequencement in linkage disequilibrium. The age of an allele can be determined from whether the allele is shared between ethnic human groups and/or between humans and related species.

DETAILED DESCRIPTION

[0027] The invention provides a substantial collection of novel polymorphisms in several genes encoding products known or suspected to have roles in biochemical pathways relating to blood pressure. Detection of polymorphisms in such genes is useful in designing and performing diagnostic assays for hypertension. Analysis of polymorphisms is also useful in designing prophylactic and therapeutic regimes customized to underlying abnormalities. As with other human polymorphisms, the polymorphisms of the invention also have more general applications, such as forensics, paternity testing, linkage analysis and positional cloning.

I. Novel Polymorphisms of the Invention.

[0028] The invention provides polymorphic sites in 75 candidate genes, known or suspected to have roles in hypertension. A gene was designated a candidate based on known or suggested involvement in blood pressure homeostasis and/or hypertension in one of the following biochemical pathways: renin-angiotensin, neural, or hormonal pathways

regulating blood pressure; regulation of vascular constriction, growth, and repair; ion and other small molecule transportation pathways in the kidney; and, regulation of glucose metabolism. Experimental evidence supporting selection of candidate genes included blood pressure physiology, animal models with altered blood pressure (including transgenic and knockout mouse or rat animal models), and human genetic linkage and association studies.

[0029] To maximize the chances of identifying informative single nucleotide polymorphisms (SNPs), DNA samples from 40 Africans and 35 US. individuals of Northern European descent were screened to include both a range of human genetic diversity and hypertension phenotype diversity. Human genetic diversity is greater within African, as compared to European, Asian or American, populations (*The History and Geography of Human Genes* (Cavalli-Sforza et al., Eds.,Princeton University Press, Princeton, NJ, 1994)). There are also significant differences in the prevalence and phenotype of hypertension between Africans (orUS Blacks) and Northern Europeans (or US Whites). Hypertension has a greater prevalence, an earlier onset and a higher frequency of salt-sensitive cases in populations of African descent. The individuals sampled were selected from the top and bottom 2.5th percentile of a normalized blood pressure distribution. Regression analysis was performed within each community sample, of systolic, diastolic and mean arterial blood pressure against age and sex, and calculated the ranked frequency distribution of residuals. Equal numbers of individuals were selected from both ends of this latter distribution to maximize potential genetic differences it the genes screened for SNPs.

[0030] 874 SNPs in 75 individuals were identified at a frequency of one SNP per 217 bases. 387 SNPs were in coding sequences, 150 in introns, and 337 in 5' and 3' UTRs. Of coding sequence chances, 178 and 209 SNPs led to synonymous and nonsynonymouse substitutions in the translated protein. On average, 12 SNPs were identified per gene, with the number ranging from zero (HSD11) to 54 (PGIS), with ten genes harboring 20 or more SNPs.

[0031] A large collection of polymorphisms of the invention are listed in Table 1. The first column of the Table 1 lists the gene and exon in which a given polymorphism occurs. For example, ACEEX13 means that a polymorphism occurs in exon 13 of angiotensin I-converting enzyme. AGTEX2 means that a polymorphism occurs in exon 2 of the angiotensinogen gene. The full names of the 75 genes shown in Table 1 are shown in Table 3. Sequences of each of the genes are available at http//www.ncbi.nlm.nih.gov/Entrez/nucleotide.html. The second column of Table 1 shows the position of a polymorphism. Numbering of nucleotides follows that of previously published reference sequences with nucleotides in sequence tags shown in column 8 being assigned the same number as the corresponding nucleotide in a reference sequence when the two are maximally aligned. In general, nucleotides in exons are numbered consecutively from the first base of the exon. Column 3 shows the base occupying the polymorphic position in a previously published sequence (arbitrarily designated a reference sequence). Column 4 of Table 1 shows the population frequency of the reference allele. For example at position 138 of exon 13 of ACE, a C nucleotide occurs in 63% of the population. Column 5 of the table shows a nucleotide occupying a polymorphic position that differs from previously published sequences. An allele containing such a nucleotide is designated an alternative allele. Column 6 of the Table shows the population frequency of the alternative allele. Column 7 of the Table shows the population frequency of heterozygosity at a polymorphic position. For example, for the polymorphic position at position 138 of exon 13 of the ACE gene, 37% of the human population are heterozygous. A high frequency of heterozygosity is advantageous in many applications of polymorphisms. The eighth column of the table shows a polymorphic position and about 15 nucleotides of flanking sequence on either side. The bases occupying the polymorphic position are indicated using IUPAC ambiguity nomenclature. For polymorphisms occurring in coding regions, columns 9 and 10 of the Table indicate the codons of the reference and alternate alleles including the polymorphic site. These columns are left blank for polymorphisms occurring in noncoding regions. Column 11 indicates whether the change between reference and alternate alleles is synonymous (i.e., no amino acid substitution due to polymorphic variation), nonsynonymous (i.e, polymorphic variation causes amino acid substitution). If the polymoprhic site does not occur in a coding region, column 11 characterizes the polymorphic site as "other." For polymorphic sites occurring in noncoding regions column 12 indicates the type of region in which the site occurs (e.g., 5' UTR, intron). For polymorphic sites occurring in coding regions, column 12 indicates the amino acid encoded by the codon of the reference allele in which the polymorphic site occurs. Column 13 indicates the amino acid encoded by the codon of the alternative allele in which the polymorphic site occurs.

[0032] The polymorphisms shown in Tables 1 were identified by resequencing of target sequences from unrelated individuals of diverse ethnic and geographic backgrounds by hybridization to probes immobilized to microfabricated arrays. About 190 kb of genomic sequence from 75 candidate genes in 75 humans (150 alleles) or about 28 MB total was analyze. The sequence included 87 kb coding DNA, 25 kb intron and 77 kb of 5' and 3' UTR sequences. Multiple target sequences from an individual were amplified from human genomic DNA using primers complementary to published sequences. The amplified target sequences were fluorescently labelled during or after PCR.

[0033] Polymorphisms were identified by hybridization of amplified DNA to arrays of oligonucleotide probes. Each genomic region was amplified by the polymerase chain reaction (PCR) in multiple segments , ranging from 80 bp to 14 kb, by both conventional and long PCR protocols. 205 distinct PCR products, averaging 3 kb, representing all 75 genes were pooled for each individual for each chip design

[0034] The strategy and principles for design and use of arrays of oligonucleotide probes are generally described in

WO 95/11995. The strategy provides arrays of probes for analysis of target sequences showing a high degree of sequence identity to the published sequences described above. A typical probe array used in this analysis has two groups of four sets of probes that respectively tile both strands of a reference sequence. A first probe set comprises a plurality of probes exhibiting perfect complementarily with one of the reference sequences. Each probe in the first probe set has an interrogation position that corresponds to a nucleotide in the reference sequence. That is, the interrogation position is aligned with the corresponding nucleotide in the reference sequence, when the probe and reference sequence are aligned to maximize complementarily between the two. For each probe in the first set, there are three corresponding probes from three additional probe sets. Thus, there are four probes corresponding to each nucleotide in the reference sequence. The probes from the three additional probe sets are identical to the corresponding probe from the first probe set except at the interrogation position, which occurs in the same position in each of the four corresponding probes from the four probe sets, and is occupied by a different nucleotide in the four probe sets. Arrays tiled for multiple different references sequences were included on the same substrate.

[0035] The labelled target sequences were hybridized with a substrate bearing immobilized arrays of probes. The amount of label bound to probes was measured. Analysis of the pattern of label revealed the nature and position of differences between the target and reference sequence. For example, comparison of the intensities of four corresponding probes reveals the identity of a corresponding nucleotide in the target sequences aligned with the interrogation position of the probes. The corresponding nucleotide is the complement of the nucleotide occupying the interrogation position of the probe showing the highest intensity (see WO 95/11995). The existence of a polymorphism is also manifested by differences in normalized hybridization intensities of probes flanking the polymorphism when the probes hybridized to corresponding targets from different individuals. For example, relative loss of hybridization intensity in a "footprint" of probes flanking a polymorphism signals a difference between the target and reference (i.e., a polymorphism) (see EP 717,113, incorporated by reference in its entirety for all purposes). Additionally, hybridization intensities for corresponding targets from different individuals can be classified into groups or clusters suggested by the data, not defined a priori, such that isolates in a give cluster tend to be similar and isolates in different clusters tend to be dissimilar. See WO 97/29212, filed February 7, 1997 (incorporated by reference in its entirety for all purposes). Hybridizations to samples from different individuals were performed separately.

II. Analysis of Polymorphisms

A. Preparation of Samples

[0036] Polymorphisms are detected in a target nucleic acid from an individual being analyzed. For assay of genomic DNA, virtually any biological sample (other than pure red blood cells) is suitable. For example, convenient tissue samples include whole blood, semen, saliva, tears, urine, fecal material, sweat, buccal, skin and hair. For assay of cDNA or mRNA, the tissue sample must be obtained from an organ in which the target nucleic acid is expressed.

[0037] Many of the methods described below require amplification of DNA from target samples. This can be accomplished by e.g., PCR. See generally PCR Technology: Principles and Applications for DNA Amplification (ed. H.A. Erlich, Freeman Press, NY, NY, 1992); PCR Protocols: A Guide to Methods and Applications (eds. Innis, et al., Academic Press, San Diego, CA, 1990); Mattila et al., Nucleic Acids Res. 19, 4967 (1991); Eckert et al., PCR Methods and Applications 1, 17 (1991); PCR (eds. McPherson et al., IRL Press, Oxford); and U.S. Patent 4,683,202 (each of which is incorporated by reference for all purposes).

[0038] Other suitable amplification methods include the ligase chain reaction (LCR) (see Wu and Wallace, Genomics 4, 560 (1989), Landegren et al., Science 241, 1077 (1988), transcription amplification (Kwoh et al., Proc. Natl. Acad. Sci. USA 86, 1173 (1989)), and self-sustained sequence replication (Guatelli et al., Proc. Nat. Acad. Sci. USA, 87, 1874 (1990)) and nucleic acid based sequence amplification (NASBA). The latter two amplification methods involve isothermal reactions based on isothermal transcription, which produce both single stranded RNA (ssRNA) and double stranded DNA (dsDNA) as the amplification products in a ratio of about 30 or 100 to 1, respectively.

B. Detection of Polymorphisms in Target DNA

[0039] The identity of bases occupying the polymorphic sites shown in Table 1 can be determined in an individual (e.g., a patient being analyzed) by several methods, which are described in turn.

1. Allele-Specific Probes

[0040] The design and use of allele-specific probes for analyzing polymorphisms is described by e.g., Saiki et al., Nature 324, 163-166 (1986); Dattagupta, EP 235,726, Saiki, WO 89/11548. Allele-specific probes can be designed that hybridize to a segment of target DNA from one individual but do not hybridize to the corresponding segment from

another individual due to the presence of different polymorphic forms in the respective segments from the two individuals. Hybridization conditions should be sufficiently stringent that there is a significant difference in hybridization intensity between alleles, and preferably an essentially binary response, whereby a probe hybridizes to only one of the alleles. Some probes are designed to hybridize to a segment of target DNA such that the polymorphic site aligns with a central position (e.g., in a 15 mer at the 7 position; in a 16 mer, at either the 8 or 9 position) of the probe. This design of probe achieves good discrimination in hybridization between different allelic forms.

[0041] Allele-specific probes are often used in pairs, one member of a pair showing a perfect match to a reference form of a target sequence and the other member showing a perfect match to a variant form. Several pairs of probes can then be immobilized on the same support for simultaneous analysis of multiple polymorphisms within the same target sequence.

2. Tiling Arrays

[0042] The polymorphisms can also be identified by hybridization to nucleic acid arrays, some example of which are described by WO 95/11995 (incorporated by reference in its entirety for all purposes). One form of such arrays is described in the Examples section in connection with de novo identification of polymorphisms. The same array or a different array can be used for analysis of characterized polymorphisms. WO 95/11995 also describes subarrays that are optimized for detection of a variant forms of a precharacterized polymorphism. Such a subarray contains probes designed to be complementary to a second reference sequence, which is an allelic variant of the first reference sequence. The second group of probes is designed by the same principles as described in the Examples except that the probes exhibit complementarily to the second reference sequence. The inclusion of a second group (or further groups) can be particular useful for analyzing short subsequences of the primary reference sequence in which multiple mutations are expected to occur within a short distance commensurate with the length of the probes (i.e., two or more mutations within 9 to 21 bases).

3. Allele-Specific Primers

[0043] An allele-specific primer hybridizes to a site on target DNA overlapping a polymorphism and only primes amplification of an allelic form to which the primer exhibits perfect complementarily. See Gibbs, Nucleic Acid Res. 17, 2427-2448 (1989). This primer is used in conjunction with a second primer which hybridizes at a distal site. Amplification proceeds from the two primers leading to a detectable product signifying the particular allelic form is present. A control is usually performed with a second pair of primers, one of which shows a single base mismatch at the polymorphic site and the other of which exhibits perfect complementarily to a distal site. The single-base mismatch prevents amplification and no detectable product is formed. The method works best when the mismatch is included in the 3'-most position of the oligonucleotide aligned with the polymorphism because this position is most destabilizing to elongation from the primer. See, e.g., WO 93/22456.

4. Direct-Sequencing

[0044] The direct analysis of the sequence of polymorphisms of the present invention can be accomplished using either the dideoxy- chain termination method or the Maxam -Gilbert method (see Sambrook et al., Molecular Cloning, A Laboratory Manual (2nd Ed., CSHP, New York 1989); Zyskind et al., Recombinant DNA Laboratory Manual, (Acad. Press, 1988)).

5. Denaturing Gradient Gel Electrophoresis

[0045] Amplification products generated using the polymerase chain reaction can be analyzed by the use of denaturing gradient gel electrophoresis. Different alleles can be identified based on the different sequence-dependent melting properties and electrophoretic migration of DNA in solution. Erlich, ed., PCR Technology, Principles and Applications for DNA Amplification, (W.H. Freeman and Co, New York, 1992), Chapter 7.

6. Single-Strand Conformation Polymorphism Analysis

[0046] Alleles of target sequences can be differentiated using single-strand conformation polymorphism analysis, which identifies base differences by alteration in electrophoretic migration of single stranded PCR products, as described in Orita et al., Proc. Nat. Acad. Sci. 86, 2766-2770 (1989). Amplified PCR products can be generated as described above, and heated or otherwise denatured, to form single stranded amplification products. Single-stranded nucleic acids may refold or form secondary structures which are partially dependent on the base sequence. The different

electrophoretic mobilities of single-stranded amplification products can be related to base-sequence difference between alleles of target sequences.

III. Methods of Use

[0047] After determining polymorphic form(s) present in an individual at one or more polymorphic sites, this information can be used in a number of methods.

A. Association Studies with Hypertension

[0048] The polymorphisms of the invention may contribute to the phenotype of an organism in different ways. Some polymorphisms occur within a protein coding sequence and contribute to phenotype by affecting protein structure. The effect may be neutral, beneficial or detrimental, or both beneficial and detrimental, depending on the circumstances. By analogy, a heterozygous sickle cell mutation confers resistance to malaria, but a homozygous sickle cell mutation is usually lethal. Other polymorphisms occur in noncoding regions but may exert phenotypic effects indirectly via influence on replication, transcription, and translation. A single polymorphism may affect more than one phenotypic trait. Likewise, a single phenotypic trait may be affected by polymorphisms in different genes. Further, some polymorphisms predispose an individual to a distinct mutation that is causally related to a certain phenotype.

[0049] The polymorphism shown in Table 1 are analyzed for a correlation with hypertension, the metabolic processes that lead to hypertension, and response to drugs used to treat hypertension. For purposes of these studies, hypertension can be defined as a dichotomous trait (e.g., diastolic blood pressure greater than 90 mm Hg), as a continuous scale of increasing severity based on blood pressure values, or as several intermediate phenotypes. Because it is likely that the causation of hypertension in the population is heterogenous, use of intermediate phenotypes can increase the strength of correlations identified. Some useful subtypes for association studies are mendelian forms of human hypertension, forms characterized by increased erythrocyte sodium-lithium countertransport, forms characterized by altered urinary kallikrein levels, and forms characterized by sensitivity of blood pressure to increases or decreases in sodium intake.

[0050] Correlation is performed for a population of individuals who have been tested for the presence or absence of hypertension or an intermediate phenotype and for one or polymorphic markers. To perform such analysis, the presence or absence of a set of polymorphic forms (i.e. a polymorphic set) is determined for a set of the individuals, some of whom exhibit a particular trait, and some of which exhibit lack of the trait. The alleles of each polymorphism of the set are then reviewed to determine whether the presence or absence of a particular allele is associated with the trait of interest. Correlation can be performed by standard statistical methods such as a K-squared test and statistically significant correlations between polymorphic form(s) and phenotypic characteristics are noted. For example, it might be found that the presence of allele A1 at polymorphism A correlates with hypertension as a dichotomous trait. As a further example, it might be found that the combined presence of allele A1 at polymorphism A and allele B1 at polymorphism B correlates with increased erythrocyte sodium lithium counter transport, an intermediate phenotype in development of hypertension.

B. Diagnosis of Hypertension

[0051] Polymorphic forms that correlate with hypertension or intermediate phenotypes are useful in diagnosing hypertension or susceptibility thereto. Combined detection of several such polymorphic forms (for example, 2, 5, 10 or 20 of the polymorphisms listed in Table 1) typically increases the probability of an accurate diagnosis. For example, the presence of a single polymorphic form known to correlate with hypertension might indicate a probability of 20% that an individual has or is susceptible to hypertension, whereas detection of five polymorphic forms, each of which correlates with hypertension, might indicate a probability of 80% that an individual has or is susceptible to hypertension. Analysis of the polymorphisms of the invention can be combined with that of other polymorphisms or other risk factors of hypertension, such as family history or obesity, as well as measurements of blood pressure.

[0052] Patients diagnosed with hypertension can be treated with conventional therapies and/or can be counselled to undertake remedial life style changes, such as a low fat, low salt diet or more exercise. Conventional therapies include diuretics (e.g., thiazides), which lower blood pressure by depleting the body of sodium and reducing blood volume; sympathoplegic agents (e.g., methyldopa and clonidine), which lower blood pressure by reducing peripheral vascular resistance, inhibiting cardiac function and increasing venous pooling in capacitance vessels; direct vasodilators (e.g., hydralazine, minoxidil,, diazoxide and sodium nitroprusside), which reduce pressure by relaxing vascular smooth muscle; agents that block production or action of angiotensin (e.g., captopril, enalapril and lisinopril), and thereby reduce peripheral vascular resistance; and adrenergic neuron blocking agents (e.g., guanethidine, reserpine, propranolol) which prevent release of norepinephrine. See, e.g., Basic and Clinical Pharmacology (Ed. Katzung, Ap-

pleton & Lange, CT, 1989).

C. Drug Screening

[0053] The polymorphism(s) showing the strongest correlation with hypertension within a given gene are likely to have a causative role in hypertension. Such a role can be confirmed by producing a transgenic animal expressing a human gene bearing such a polymorphism and determining whether the animal develops hypertension. Polymorphisms in coding regions that result in amino acid changes usually cause hypertension by decreasing, increasing or otherwise altering the activity of the protein encoded by the gene in which the polymorphism occurs. Polymorphisms in coding regions that introduce stop codons usually cause hypertension by reducing (heterozygote) or eliminating (homozygote) functional protein produced by the gene. Occasionally, stop codons result in production of a truncated peptide with aberrant activities relative to the full-length protein. Polymorphisms in regulatory regions typically cause hypertension by causing increased or decreased expression of the protein encoded by the gene in which the polymorphism occurs. Polymorphisms in intronic sequences can cause hypertension either through the same mechanism as polymorphisms in regulatory sequences or by causing altered spliced patterns resulting in an altered protein. For example, alternative splice patterns have been reported for the human angiotensin II receptor gene (Curnow et al., Molecular Endocrinology 9, 1250-1262 (1995)).

[0054] The precise role of polymorphisms in hypertension can be elucidated by several means. Alterations in expression levels of a protein (e.g., sodium-calcium ion channel) can be determined by measuring protein levels in samples groups of persons characterized as having or not having hypertension (or intermediate phenotypes). Alterations in enzyme activity (e.g., renin), can similarly be detected by assaying for enzyme activity in samples from the above groups of persons. Alterations in receptor transducing activity (e.g., angiotensin II receptor, β-3-adrenergic receptor or bradykinin receptor B2) can be detected by comparing receptor ligand binding, either in vitro or in a cellular expression system.

[0055] Having identified certain polymorphisms as having causative roles in hypertension, and having elucidated at least in general terms whether such polymorphisms increase or decrease the activity or expression level of associated proteins, customized therapies can be devised for classes of patients with different genetic subtypes of hypertension. For example, if a polymorphism in a given protein causes hypertension by increasing the expression level or activity of the protein, hypertension associated with the polymorphism can be treated by administering an antagonist of the protein. If a polymorphism in a given protein causes hypertension by decreasing the expression level or activity of a protein, the form of hypertension associated with the polymorphism can be treated by administering the protein itself, a nucleic acid encoding the protein that can be expressed in a patient, or an analog or agonist of the protein.

[0056] Agonists, antagonists can be obtained by producing and screening large combinatorial libraries. Combinatorial libraries can be produced for many types of compound that can be synthesized in a step by step fashion. Such compounds include polypeptides, beta-turn mimetics, polysaccharides, phospholipids, hormones, prostaglandins, steroids, aromatic compounds, heterocyclic compounds, benzodiazepines, oligomeric N-substituted glycines and oligocarbamates. Large combinatorial libraries of the compounds can be constructed by the encoded synthetic libraries (ESL) method described in Affymax, WO 95/12608, Affymax, WO 93/06121, Columbia University, WO 94/08051, Pharmacopeia, WO 95/35503 and Scripps, WO 95/30642 (each of which is incorporated by reference for all purposes). Peptide libraries can also be generated by phage display methods. See, e.g., Devlin, W0 91/18980. The libraries of compounds can be initially screened for specific binding to the protein for which agonists or antagonists are to be identified, or to its natural binding partner. Preferred agents bind with a Kd < μM. For example, for receptor ligand combinations, the assay can be performed using cloned receptor immobilized to a support such as a microtiter well and binding of compounds can be measured in competition with ligand to the receptor. Agonist or antagonist activity can then be assayed using a cellular reporter system or a transgenic animal model.

[0057] The polymorphisms of the invention are also useful for conducting clinical trials of drug candidates for hypertension. Such trials are performed on treated or control populations having similar or identical polymorphic profiles at a defined collection of polymorphic sites. Use of genetically matched populations eliminates or reduces variation in treatment outcome due to genetic factors, leading to a more accurate assessment of the efficacy of a potential drug.

D. Other Diseases

[0058] The polymorphisms in Table 1 can also be tested for association with other disease that have known but hitherto unmapped genetic components (e.g., agammaglobulinemia, diabetes insipidus, Lesch-Nyhan syndrome, muscular dystrophy, Wiskott-Aldrich syndrome, Fabry's disease, familial hypercholesterolemia, polycystic kidney disease, hereditary spherocytosis, von Willebrand's disease, tuberous sclerosis, hereditary hemorrhagica telangiectasia, familial colonic polyposis, Ehlers-Danlos syndrome, osteogenesis imperfecta, and acute intermittent porphyria). Phenotypic traits also include symptoms of, or susceptibility to, multifactorial diseases of which a component is or may be genetic,

such as autoimmune diseases, inflammation, cancer, diseases of the nervous system, and infection by pathogenic microorganisms. Some examples of autoimmune diseases include rheumatoid arthritis, multiple sclerosis, diabetes (insulin-dependent and non-independent), systemic lupus erythematosus and Graves disease. Some examples of cancers include cancers of the bladder, brain, breast, colon, esophagus, kidney, leukemia, liver, lung, oral cavity, ovary, pancreas, prostate, skin, stomach and uterus. Phenotypic traits also include characteristics such as longevity, appearance (e.g., baldness, obesity), strength, speed, endurance, fertility, and susceptibility or receptivity to particular drugs or therapeutic treatments.

[0059] Such correlations can be exploited in several ways. In the case of a strong correlation between a set of one or more polymorphic forms and a disease for which treatment is available, detection of the polymorphic form set in a human or animal patient may justify immediate administration of treatment, or at least the institution of regular monitoring of the patient. Detection of a polymorphic form correlated with serious disease in a couple contemplating a family may also be valuable to the couple in their reproductive decisions. For example, the female partner might elect to undergo in vitro fertilization to avoid the possibility of transmitting such a polymorphism from her husband to her offspring. In the case of a weaker, but still statistically significant correlation between a polymorphic set and human disease, immediate therapeutic intervention or monitoring may not be justified. Nevertheless, the patient can be motivated to begin simple life-style changes (e.g., diet, exercise) that can be accomplished at little cost to the patient but confer potential benefits in reducing the risk of conditions to which the patient may have increased susceptibility by virtue of variant alleles. Identification of a polymorphic set in a patient correlated with enhanced receptiveness to one of several treatment regimes for a disease indicates that this treatment regime should be followed.

E. Forensics

[0060] Determination of which polymorphic forms occupy a set of polymorphic sites in an individual identifies a set of polymorphic forms that distinguishes the individual. See generally National Research Council, The Evaluation of Forensic DNA Evidence (Eds. Pollard et al., National Academy Press, DC, 1996). The more sites that are analyzed the lower the probability that the set of polymorphic forms in one individual is the same as that in an unrelated individual. Preferably, if multiple sites are analyzed, the sites are unlinked. Thus, polymorphisms of the invention are often used in conjunction with polymorphisms in distal genes. Preferred polymorphisms for use in forensics are diallelic because the population frequencies of two polymorphic forms can usually be determined with greater accuracy than those of multiple polymorphic forms at multi-allelic loci.

[0061] The capacity to identify a distinguishing or unique set of forensic markers in an individual is useful for forensic analysis. For example, one can determine whether a blood sample from a suspect matches a blood or other tissue sample from a crime scene by determining whether the set of polymorphic forms occupying selected polymorphic sites is the same in the suspect and the sample. If the set of polymorphic markers does not match between a suspect and a sample, it can be concluded (barring experimental error) that the suspect was not the source of the sample. If the set of markers does match, one can conclude that the DNA from the suspect is consistent with that found at the crime scene. If frequencies of the polymorphic forms at the loci tested have been determined (e.g., by analysis of a suitable population of individuals), one can perform a statistical analysis to determine the probability that a match of suspect and crime scene sample would occur by chance.

[0062] p(ID) is the probability that two random individuals have the same polymorphic or allelic form at a given polymorphic site. In diallelic loci, four genotypes are possible: AA, AB, BA, and BB. If alleles A and B occur in a haploid genome of the organism with frequencies x and y, the probability of each genotype in a diploid organism are (see WO 95/12607):

Homozygote: p(AA)= x2
Homozygote: p(BB)= y2 = (1-x)2
Single Heterozygote: p(AB)= p(BA)= xy = x(1-x)
Both Heterozygotes: p(AB+BA)= 2xy = 2x(1-x)

[0063] The probability of identity at one locus (i.e, the probability that two individuals, picked at random from a population will have identical polymorphic forms at a given locus) is given by the equation:

$$p(ID) = (x2)2 + (2xy)2 + (y2)2.$$

[0064] These calculations can be extended for any number of polymorphic forms at a given locus. For example, the probability of identity p(ID) for a 3-allele system where the alleles have the frequencies in the population of x, y and z, respectively, is equal to the sum of the squares of the genotype frequencies:

$$p(ID) = x4 + (2xy)2 + (2yz)2 + (2xz)2 + z4 + y4$$

[0065] In a locus of n alleles, the appropriate binomial expansion is used to calculate p(ID) and p(exc).

[0066] The cumulative probability of identity (cum p(ID)) for each of multiple unlinked loci is determined by multiplying the probabilities provided by each locus.

$$\text{cum } p(ID) = p(ID1)p(ID2)p(ID3).... \; p(IDn)$$

[0067] The cumulative probability of non-identity for n loci (i.e. the probability that two random individuals will be different at 1 or more loci) is given by the equation:

$$\text{cum } p(nonID) = 1\text{-cum } p(ID).$$

[0068] If several polymorphic loci are tested, the cumulative probability of non-identity for random individuals becomes very high (e.g., one billion to one). Such probabilities can be taken into account together with other evidence in determining the guilt or innocence of the suspect.

F. Paternity Testing

[0069] The object of paternity testing is usually to determine whether a male is the father of a child. In most cases, the mother of the child is known and thus, the mother's contribution to the child's genotype can be traced. Paternity testing investigates whether the part of the child's genotype not attributable to the mother is consistent with that of the putative father. Paternity testing can be performed by analyzing sets of polymorphisms in the putative father and the child.

[0070] If the set of polymorphisms in the child attributable to the father does not match the putative father, it can be concluded, barring experimental error, that the putative father is not the real father. If the set of polymorphisms in the child attributable to the father does match the set of polymorphisms of the putative father, a statistical calculation can be performed to determine the probability of coincidental match.

[0071] The probability of parentage exclusion (representing the probability that a random male will have a polymorphic form at a given polymorphic site that makes him incompatible as the father) is given by the equation (see WO 95/12607):

$$p(exc) = xy(1\text{-}xy)$$

where x and y are the population frequencies of alleles A and B of a diallelic polymorphic site.

[0072] (At a triallelic site $p(exc) = xy(1\text{-}xy) + yz(1\text{-}yz) + xz(1\text{-}xz) + 3xyz(1\text{-}xyz)$)), where x, y and z and the respective population frequencies of alleles A, B and C).

[0073] The probability of non-exclusion is

$$p(\text{non-exc}) = 1\text{-}p(exc)$$

[0074] The cumulative probability of non-exclusion (representing the value obtained when n loci are used) is thus:

$$\text{cum } p(\text{non-exc}) = p(\text{non-exc1})p(\text{non-exc2})p(\text{non-exc3}).... \; p(\text{non-excn})$$

[0075] The cumulative probability of exclusion for n loci (representing the probability that a random male will be excluded)

$$\text{cum } p(exc) = 1 - \text{cum } p(\text{non-exc}).$$

[0076] If several polymorphic loci are included in the analysis, the cumulative probability of exclusion of a random

male is very high. This probability can be taken into account in assessing the liability of a putative father whose polymorphic marker set matches the child's polymorphic marker set attributable to his/her father.

G. Genetic Mapping of Phenotypic Traits

[0077] The polymorphisms shown in table 1 can also be used to establish physical linkage between a genetic locus associated with a trait of interest and polymorphic markers that are not associated with the trait, but are in physical proximity with the genetic locus responsible for the trait and co-segregate with it. Such analysis is useful for mapping a genetic locus associated with a phenotypic trait to a chromosomal position, and thereby cloning gene(s) responsible for the trait. See Lander et al., Proc. Natl. Acad. Sci. (USA) 83, 7353--7357 (1986); Lander et al., Proc. Natl. Acad. Sci. (USA) 84, 2363-2367 (1987); Donis-Keller et al., Cell 51, 319-337 (1987); Lander et al., Genetics 121, 185-199 (1989)). Genes localized by linkage can be cloned by a process known as directional cloning. See Wainwright, Med. J. Australia 159, 170-174 (1993); Collins, Nature Genetics 1, 3-6 (1992) (each of which is incorporated by reference in its entirety for all purposes).

[0078] Linkage studies are typically performed on members of a family. Available members of the family are characterized for the presence or absence of a phenotypic trait and for a set of polymorphic markers. The distribution of polymorphic markers in an informative meiosis is then analyzed to determine which polymorphic markers co-segregate with a phenotypic trait. See, e.g., Kerem et al., Science 245, 1073-1080 (1989); Monaco et al., Nature 316, 842 (1985); Yamoka et al., Neurology 40, 222-226 (1990); Rossiter et al., FASEB Journal 5, 21-27 (1991).

[0079] Linkage is analyzed by calculation of LOD (log of the odds) values. A lod value is the relative likelihood of obtaining observed segregation data for a marker and a genetic locus when the two are located at a recombination fraction θ. versus the situation in which the two are not linked, and thus segregating independently (Thompson & Thompson. Genetics in Medicine (5th ed, W.B. Saunders Company, Philadelphia, 1991); Strachan, "Mapping the human genome" in The Human Genome (BIOS Scientific Publishers Ltd, Oxford), Chapter 4). A series of likelihood ratios are calculated at various recombination fractions (θ), ranging from $\theta = 0.0$ (coincident loci) to $\theta = 0.50$ (unlinked). Thus, the likelihood at a given value of θ is: probability of data if loci linked at θ to probability of data if loci unlinked. The computed likelihoods are usually expressed as the log10 of this ratio (i.e., a lod score). For example, a lod score of 3 indicates 1000:1 odds against an apparent observed linkage being a coincidence. The use of logarithms allows data collected from different families to be combined by simple addition. Computer programs are available for the calculation of lod scores for differing values of θ (e.g., LIPED, MLINK (Lathrop, Proc. Nat. Acad. Sci. (USA) 81, 3443-3446 (1984)). For any particular lod score, a recombination fraction may be determined from mathematical tables. See Smith et al., Mathematical tables for research workers in human genetics (Churchill, London, 1961); Smith, Ann. Hum. Genet. 32, 127-150 (1968). The value of θ at which the lod score is the highest is considered to be the best estimate of the recombination fraction. Positive lod score values suggest that the two loci are linked, whereas negative values suggest that linkage is less likely (at that value of θ) than the possibility that the two loci are unlinked. By convention, a combined lod score of +3 or greater (equivalent to greater than 1000:1 odds in favor of linkage) is considered definitive evidence that two loci are linked. Similarly, by convention, a negative lod score of -2 or less is taken as definitive evidence against linkage of the two loci being compared. Negative linkage data are useful in excluding a chromosome or a segment thereof from consideration. The search focuses on the remaining non-excluded chromosomal locations.

IV. Modified Polypeptides and Gene Sequences

[0080] The invention further provides variant forms of nucleic acids and corresponding proteins. The nucleic acids comprise one of the sequences described in Table 1, column 8, in which the polymorphic position is occupied by an alternative base for that position. Some nucleic acid encode full-length variant forms of proteins. Similarly, variant proteins have the prototypical amino acid sequences of encoded by nucleic acid sequence shown in Table 1, column 8, (read so as to be in-frame with the full-length coding sequence of which it is a component) except at an amino acid encoded by a codon including one of the polymorphic positions shown in the Table. That position is occupied by the amino acid coded by the corresponding codon in the alternative forms shown in the Table.

[0081] Variant genes can be expressed in an expression vector in which a variant gene is operably linked to a native or other promoter. Usually, the promoter is a eukaryotic promoter for expression in a mammalian cell. The transcription regulation sequences typically include a heterologous promoter and optionally an enhancer which is recognized by the host. The selection of an appropriate promoter, for example trp, lac, phage promoters, glycolytic enzyme promoters and tRNA promoters, depends on the host selected. Commercially available expression vectors can be used. Vectors can include host-recognized replication systems, amplifiable genes, selectable markers, host sequences useful for insertion into the host genome, and the like.

[0082] The means of introducing the expression construct into a host cell varies depending upon the particular construction and the target host. Suitable means include fusion, conjugation, transfection, transduction, electroporation

or injection, as described in Sambrook, supra. A wide variety of host cells can be employed for expression of the variant gene, both prokaryotic and eukaryotic. Suitable host cells include bacteria such as E. coli, yeast, filamentous fungi, insect cells, mammalian cells, typically immortalized, e.g., mouse, CHO, human and monkey cell lines and derivatives thereof. Preferred host cells are able to process the variant gene product to produce an appropriate mature polypeptide. Processing includes glycosylation, ubiquitination, disulfide bond formation, general post-translational modification, and the like.

[0083] The protein may be isolated by conventional means of protein biochemistry and purification to obtain a substantially pure product, i.e., 80, 95 or 99% free of cell component contaminants, as described in Jacoby, Methods in Enzymology Volume 104, Academic Press, New York (1984); Scopes, Protein Purification, Principles and Practice, 2nd Edition, Springer-Verlag, New York (1987); and Deutscher (ed), Guide to Protein Purification, Methods in Enzymology, Vol. 182 (1990). If the protein is secreted, it can be isolated from the supernatant in which the host cell is grown. If not secreted, the protein can be isolated from a lysate of the host cells.

[0084] The invention further provides transgenic nonhuman animals capable of expressing an exogenous variant gene and/or having one or both alleles of an endogenous variant gene inactivated. Expression of an exogenous variant gene is usually achieved by operably linking the gene to a promoter and optionally an enhancer, and microinjecting the construct into a zygote. See Hogan et al., "Manipulating the Mouse Embryo, A Laboratory Manual," Cold Spring Harbor Laboratory. Inactivation of endogenous variant genes can be achieved by forming a transgene in which a cloned variant gene is inactivated by insertion of a positive selection marker. See Capecchi, Science 244, 1288-1292 (1989). The transgene is then introduced into an embryonic stem cell, where it undergoes homologous recombination with an endogenous variant gene. Mice and other rodents are preferred animals. Such animals provide useful drug screening systems.

[0085] In addition to substantially full-length polypeptides expressed by variant genes, the present invention includes biologically active fragments of the polypeptides, or analogs thereof, including organic molecules which simulate the interactions of the peptides. Biologically active fragments include any portion of the full-length polypeptide which confers a biological function on the variant gene product, including ligand binding, and antibody binding. Ligand binding includes binding by nucleic acids, proteins or polypeptides, small biologically active molecules, or large cellular structures.

[0086] Polyclonal and/or monoclonal antibodies that specifically bind to variant gene products but not to corresponding prototypical gene products are also provided. Antibodies can be made by injecting mice or other animals with the variant gene product or synthetic peptide fragments thereof. Monoclonal antibodies are screened as are described, for example, in Harlow & Lane, Antibodies, A Laboratory Manual, Cold Spring Harbor Press, New York (1988); Goding, Monoclonal antibodies, Principles and Practice (2d ed.) Academic Press, New York (1986). Monoclonal antibodies are tested for specific immunoreactivity with a variant gene product and lack of immunoreactivity to the corresponding prototypical gene product. These antibodies are useful in diagnostic assays for detection of the variant form, or as an active ingredient in a pharmaceutical composition.

V. Kits

[0087] The invention further provides kits comprising at least one allele-specific oligonucleotide as described above. Often, the kits contain one or more pairs of allele-specific oligonucleotides hybridizing to different forms of a polymorphism. In some kits, the allele-specific oligonucleotides are provided immobilized to a substrate. For example, the same substrate can comprise allele-specific oligonucleotide probes for detecting at least 10, 100 or all of the polymorphisms shown in Table 1. Optional additional components of the kit include, for example, restriction enzymes, reverse-transcriptase or polymerase, the substrate nucleoside triphosphates, means used to label (for example, an avidin-enzyme conjugate and enzyme substrate and chromogen if the label is biotin), and the appropriate buffers for reverse transcription, PCR, or hybridization reactions. Usually, the kit also contains instructions for carrying out the methods.

VI. Computer Systems For Storing Polymorphism Data

[0088] Fig. 1A depicts a block diagram of a computer system 10 suitable for implementing the present invention. Computer system 10 includes a bus 12 which interconnects major subsystems such as a central processor 14, a system memory 16 (typically RAM), an input/output (I/O) controller 18, an external device such as a display screen 24 via a display adapter 26, serial ports 28 and 30, a keyboard 32, a fixed disk drive 34 via a storage interface 35 and a floppy disk drive 36 operative to receive a floppy disk 38, and a CD-ROM (or DVD-ROM) device 40 operative to receive a CD-ROM 42. Many other devices can be connected such as a user pointing device, e.g., a mouse 44 connected via serial port 28 and a network interface 46 connected via serial port 30.

[0089] Many other devices or subsystems (not shown) may be connected in a similar manner. Also, it is not necessary for all of the devices shown in Fig. 1A to be present to practice the present invention, as discussed below. The devices and subsystems may be interconnected in different ways from that shown in Fig. 1A. The operation of a computer

system such as that shown in Fig. 1A is well known. Databases storing polymorphism information according to the present invention can be stored, e.g., in system memory 16 or on storage media such as fixed disk 34, floppy disk 38, or CD-ROM 42. An application program to access such databases can be operably disposed in system memory 16 or sorted on storage media such as fixed disk 34, floppy disk 38, or CD-ROM 42.

[0090] Fig. 1B depicts the interconnection of computer system 10 to remote computers 48, 50, and 52. Fig. 1B depicts a network 54 interconnecting remote servers 48, 50, and 52. Network interface 46 provides the connection from client computer system 10 to network 54. Network 54 can be, e.g., the Internet. Protocols for exchanging data via the Internet and other networks are well known. Information identifying the polymorphisms described herein can be transmitted across network 54 embedded in signals capable of traversing the physical media employed by network 54.

[0091] Information identifying polymorphisms shown in Table 1 is represented in records, which optionally, are subdivided into fields. Each record stores information relating to a different polymorphisms in Table 1. Collectively, the records can store information relating to all of the polymorphisms in Table 1, or any subset thereof, such as 5, 10, 50, or 100 polymorphisms from Table 1. In some databases, the information identifies a base occupying a polymorphic position and the location of the polymorphic position. The base can be represented as a single letter code (i.e., A, C, G or T/U) present in a polymorphic form other than that in the reference allele. Alternatively, the base occupying a polymorphic site can be represented in IUPAC ambiguity code as shown in Table 1. The location of a polymorphic site can be identified as its position within one of the sequences shown in Table 1. For example, in the first sequence shown in Table 1, the polymorphic site occupies the 15th base. The position can also be identified by reference to, for example, a chromosome, and distance from known markers within the chromosome. In other databases, information identifying a polymorphism contains sequences of 10-100 bases shown in Table 1 or the complements thereof including a polymorphic site. Preferably, such information records at least 10, 15, 20, or 30 contiguous bases of sequences including a polymorphic site.

[0092] From the foregoing, it is apparent that the invention includes a number of general uses that can be expressed concisely as follows. The invention provides for the use of any of the nucleic acid segments described above in the diagnosis or monitoring of diseases, particularly hypertension. The invention further provides for the use of any of the nucleic acid segments in the manufacture of a medicament for the treatment or prophylaxis of such diseases. The invention further provides for the use of any of the DNA segments as a pharmaceutical.

[0093] All publications and patent applications cited above are incorporated by reference in their entirety for all purposes to the same extent as if each individual publication or patent application were specifically and individually indicated to be so incorporated by reference. Although the present invention has been described in some detail by way of illustration and example for purposes of clarity and understanding, it will be apparent that certain changes and modifications may be practiced within the scope of the appended claims.

TABLE 1

Gene/Exon	Base Position	Ref Allele	Freq (P)	Alt Allele	Freq (Q)	Heterozygosity (H)	Sequence Tag	Ref Codon	Alt Codon	Type of amino acid change	Ref amino acid	Alt amino acid
AADDEX1	305	G	0.98	A	0.03	0.05	ACGGGGGCGGAGCCRGAGCCGGAGCCGAC	.	.	Other	5' UTR	.
AADDEX10	246	G	0.86	T	0.14	0.23	AAGCTTCCGAGGAAKGGCAGAATGGAAGC	GGG	TGG	Nonsynonymous	Gly	Trp
AADDEX12	43	A	0.94	T	0.06	0.11	GATCCGAGAGCAGAWTTTACAGGACATTA	AAT	ATT	Nonsynonymous	Asn	Ile
AADDEX13	173	C	0.70	G	0.30	0.42	GAAGCAGAAGGGCTSTGAAGGTGAGTGCT	TCT	TGT	Nonsynonymous	Ser	Cys
AADDEX15	74	C	0.73	T	0.27	0.40	CCTAGTAAGTACCGYGCTGCCTCCGCTCT	.	.	Other	Intron	.
AADDEX16	1071	G	0.99	A	0.01	0.02	ATTCCTGTCATAGGRAAGGTATATCAGGA	.	.	Other	3' UTR	.
AADDEX16	1321	C	0.98	T	0.02	0.04	GCCCTGGGGCCCCTYGACATCACCGTCAT	.	.	Other	3' UTR	.
AADDEX16	1328	A	0.91	G	0.09	0.17	GGCCCCTCGACATCRCCGTCATTGATGGA	.	.	Other	3' UTR	.
AADDEX16	1478	A	0.89	G	0.11	0.19	CAGCCTGACTAGGTRCAGGCAAGCTTGTG	.	.	Other	3' UTR	.
AADDEX16	691	C	0.99	G	0.01	0.02	CAGCTTTGGCTGCASGTCACCCTCCTGAG	.	.	Other	3' UTR	.
AADDEX16	995	C	0.94	T	0.06	0.11	TATGCATGTCTGACYGACGATCCCTCGAC	.	.	Other	3' UTR	.
AADDEX2	31	A	0.98	G	0.03	0.05	TTTGATTCTCGTAGGRACCTAGAAAGATTG	.	.	Other	5' UTR	.
AADDEX7	96	T	0.98	A	0.02	0.04	TTGGAGAAGTGGCTWATCATGACTACCAT	TAT	AAT	Nonsynonymous	Tyr	Asn
AADDEX9	173	A	0.93	T	0.07	0.13	ATTGGTGAGCAGGAWTTTGAAGCCCTCAT	GAA	GAT	Nonsynonymous	Glu	Asp
ACEEX13	151	T	0.75	C	0.25	0.38	CCAGCCAGGAGGCAYCCCAACAGGTGACA	TCT	CCT	Nonsynonymous	Ser	Pro
ACEEX13	202	A	0.75	G	0.25	0.38	AGGCAACAACCAGCRGCCAGACAACCACC	AGC	GGC	Nonsynonymous	Ser	Gly
ACEEX15	144	G	0.80	A	0.20	0.32	CTAGAACGGGCAGCRCTGCCTGCCCAGGA	GCG	GCA	Synonymous	Ala	Ala
ACEEX17	19	C	0.69	A	0.31	0.43	CTCAAGCCATTCAAMCCCCTACCAGATCT	.	.	Other	Intron	.
ACEEX18	130	C	0.95	G	0.05	0.09	CAGCCACTCTACCTSAACCTGCATGCCTA	CTC	CTG	Synonymous	Leu	Leu
ACEEX21	150	T	0.98	C	0.03	0.05	CTTCCATGAGGCCAYTGGGGACGTGCTAG	ATT	ACT	Nonsynonymous	Ile	Thr
ACEEX22	19	T	0.99	G	0.01	0.03	AGCATGACATCAACKTTCTGATGAAGATG	TTT	GTT	Nonsynonymous	Phe	Val
ACEEX24	118	C	0.95	T	0.05	0.10	CAGTCCAAGGAGGCYGGGCAGCGCCTGGG	GCC	GCT	Synonymous	Ala	Ala
ACEEX24	16	T	0.57	C	0.43	0.49	TGCTCCAGGTACTTYGTCAGCTTCATCAT	TTT	TTC	Synonymous	Phe	Phe
ACEEX26	154	G	0.98	A	0.03	0.05	GGGCCTCAGCCAGCRGCTCTTCAGCATCC	CGG	CAG	Nonsynonymous	Arg	Gln
ACEEX26	174	C	0.90	A	0.10	0.18	TCAGCATCCGCCACMGCAGCCTCCACCGG	CGC	AGC	Nonsynonymous	Arg	Ser

ACEEX26	205	A	0.98	C	0.02	0.03	CTCCCACGGGCCCCCMGTTCGGCTCCGAGG	CAG	CCG	Nonsynonymous	Gln	Pro
ACEEX26	224	G	0.94	A	0.06	0.11	GGCTCCGAGGTGGARCTGAGACACTCCTG	GAG	GAA	Synonymous	Glu	Glu
ADDBEX10	81	G	0.98	T	0.03	0.05	CTCCTGGAGCAGGAKAAGCACCGGCCCCA	GAG	GAT	Nonsynonymous	Glu	Asp
ADDBEX15	68	G	0.99	A	0.01	0.03	GCTCTGGTCCGGCCRTGTGCGAGTTCTTC	CCG	CCA	Synonymous	Pro	Pro
ADDBEX15	85	C	0.90	T	0.10	0.18	TGCGAGTTCTTCAGYGTTGCCCTCCACAT	GCG	GTG	Nonsynonymous	Ala	Val
ADDBEX17	147	C	0.98	A	0.02	0.04	GAGGAAATCCTCAGMAAAGGCCTGAGCCA	AGC	AGA	Nonsynonymous	Ser	Arg
ADDBEX3	138	G	0.89	A	0.11	0.19	GCTTCTCAGAGGACRACCCCGAGTACATG	GAC	AAC	Nonsynonymous	Asp	Asn
ADDBEX4	134	C	0.99	G	0.01	0.02	CATGGCCAGCACCTSCCACGCAGTCTTCC	TCC	TGC	Nonsynonymous	Ser	Cys
ADDBEX8	173	A	0.96	G	0.04	0.07	CCACCTGCAAGGTTRGCTTAGCTCTTCTG	.	.	Other	Intron	.
ADDBEX9	69	T	0.99	C	0.01	0.02	GTAGAGGAGGCATTYTACAAGATCTTCCA	TTT	TTC	Synonymous	Phe	Phe
ADDG	2087	T	0.98	C	0.02	0.03	TGACATTGCACATCYAAATACCACATTTA	.	.	Other	3' UTR	.
ADORA2AEX1	429	C	0.97	T	0.03	0.07	GGTGTCACTGGCGGYGGCCGACATCGCAG	GCG	GTG	Nonsynonymous	Ala	Val
ADORA2AEX2	1230	G	0.97	T	0.03	0.06	TGCAGAAGCATCTGKAAGCACCACCTTGT	.	.	Other	3' UTR	.
ADORA2AEX2	596	G	0.97	A	0.03	0.06	CCGCCAGACCTTCCRCAAGATCATTCGCA	CGC	CAC	Nonsynonymous	Arg	His
ADORA2AEX2	741	C	0.92	T	0.08	0.15	GGAGTGTGGGCCAAYGGCAGTGCTCCCCA	AAC	AAT	Synonymous	Asn	Asn
ADRB3EX1	1020	C	0.96	T	0.04	0.07	GGCCCCGGTGGGGAYGTGCGCTCCGCCCG	ACG	ATG	Nonsynonymous	Thr	Met
ADRB3EX1	1354	C	0.89	T	0.11	0.20	TGCGCCGCCGCCCGYCCGGCCCTCTTCCC	CGC	CGT	Synonymous	Arg	Arg
ADRB3EX1	1445	G	0.90	T	0.10	0.18	GGTAGGTAACCGGGKCCAGAGGGACCGGCG	.	.	Other	Intron	.
ADRB3EX1	44	A		G			GCTACTCCTCCCCCHAGAGCGGTGGCACC	.	.	Other	5' UTR	.
ADRB3EX2	301	G	0.96	C	0.04	0.08	GTGGTAGTGTCCAGSTGCCGTGGAGCAGC	.	.	Other	3' UTR	.
ADRB3EX2	408	C	0.80	T	0.20	0.32	TGGTTCCATTCCTTYTGCCACCCAACCC	.	.	Other	3' UTR	.
ADROMEX1	1197	C	0.98	T	0.02	0.04	TGGGACGTCTGAGAYTTTCTCCTTCAAGT	.	.	Other	5' UTR	.
ADROMEX1	154	G	0.98	T	0.02	0.05	ATGTTACCTTCCTTKCCTGACTCAAGGGT	.	.	Other	Promoter	.
ADROMEX1	723	C	0.97	T	0.03	0.06	GGGCTCTTGCTGTTYTTCGCCAGGAGGCT	.	.	Other	Promoter	.
ADROMEX1	981	G	0.99	A	0.01	0.03	GAGCAGGAGCGCGCRTGGCTGAGGAAAGA	.	.	Other	Promoter	.
ADROMEX2	101	A	0.96	C	0.04	0.07	TCGCTCGCCTTCCTMGGGCTGACACCGC	CTA	CTC	Synonymous	Leu	Leu
ADROMEX3	81	C	0.95	G	0.05	0.09	CTGCGGATGTCCAGSAGCTACCCCACCGG	AGC	AGG	Nonsynonymous	Ser	Arg
ADROMEX4	1033	T	0.95	C	0.05	0.09	ACCGAGTCTCTGTAYAATCTATTTACATA	.	.	Other	3' UTR	.
ADROMEX4	1292	A	0.98	G	0.02	0.05	TGTCCTGGGTGCGARTCAGGGCTTCGCGG	.	.	Other	3' UTR	.
ADROMEX4	1389	T	0.97	C	0.03	0.06	GCGAGCCTGGACTCYCGGGTTGCGCAACG	.	.	Other	3' UTR	.
ADROMEX4	388	G	0.98	C	0.02	0.05	CAAGCATCCCGCTGSTGCCTCCCGGGACG	.	.	Other	3' UTR	.

ADROMEX4	536	T	0.98	G	0.02	0.04	CGCTTCCTTAGCCTKGCTCAGGTGCAAGT	.	.	.	Other	3' UTR	.	.
ADROMEX4	918	A	0.91	G	0.09	0.16	ATTTTAAGACGTGARTGTCTCAGCGAGGT	.	.	.	Other	3' UTR	.	.
AE1EX1	298	G	0.95	A	0.05	0.10	GGGGCATGAGTCAGRGGTTTGCGAGCTGC	.	.	.	Other	Promoter	.	.
AE1EX1	80	A	0.98	C	0.02	0.04	TCAAACCTTCATCCMCAAAGGAAGAGTCA	.	.	.	Other	Promoter	.	.
AE1EX10	77	G	0.99	A	0.01	0.02	CGAGGGGAGCTGCTRCACTCCCTAGAGGG	CTG	CTA	.	Synonymous	Leu	Leu	Leu
AE1EX11	181	C	0.95	T	0.05	0.10	GTCATCTTCATCTAYTTTGCTGCACTGTC	TAC	TAT	.	Synonymous	Tyr	Tyr	Tyr
AE1EX11	191	C	0.99	T	0.01	0.03	TCTACTTTGCTGCAYGTGTCACCCGCCATC	CTG	TTG	.	Synonymous	Leu	Leu	Leu
AE1EX11	228	A	0.98	T	0.02	0.04	CGGCCTCCTGGGTCWGTGCCAATACCTGT	.	.	.	Other	Intron	.	.
AE1EX12	70	G	0.93	A	0.07	0.13	GTGTCGGAGCTGCTRATCTCCACTGCAGT	CTG	CTA	.	Synonymous	Leu	Leu	Leu
AE1EX12	71	A	0.96	T	0.04	0.07	TGTCGGAGCTGCTGWTCTCCACTGCAGTG	ATC	TTC	.	Nonsynonymous	Ile	Phe	Phe
AE1EX14	159	A	0.93	T	0.07	0.13	CCTTCTTCTTTGCCWTGATGCTGCGCAAG	ATG	TTG	.	Nonsynonymous	Met	Leu	Leu
AE1EX15	107	T	0.79	C	0.21	0.33	TTCTTCATTCAGGAYACCTACACCCAGGT	GAT	GAC	.	Synonymous	Asp	Asp	Asp
AE1EX16	92	C	0.97	T	0.03	0.06	GGCTGGGTCATCCAYCCACTGGGCTTGCG	CAC	CAT	.	Synonymous	His	His	His
AE1EX17	34	A	0.97	G	0.03	0.06	CCTACAGTAGGCTGRTTGTCAGCAAACCT	ATT	GTT	.	Nonsynonymous	Ile	Val	Val
AE1EX17	40	A	0.99	G	0.01	0.02	GTAGGCTGATTGTCRGCAAACCTGAGCGC	AGC	GGC	.	Nonsynonymous	Ser	Gly	Gly
AE1EX17	72	C	0.94	T	0.06	0.11	ATGGTCAAGGGCTCYGGCTTCCACCTGGA	TCC	TCT	.	Synonymous	Ser	Ser	Ser
AE1EX19	132	G	0.96	A	0.04	0.07	TGGCCCTGCCCTTCRTCCTCATCCTCACT	CGT	CAT	.	Nonsynonymous	Arg	His	His
AE1EX19	43	G	0.99	A	0.01	0.02	GGTGAAGACCTGGCRCATGCACTTATTCA	CGC	CAC	.	Nonsynonymous	Arg	His	His
AE1EX20	1007	G	0.99	A	0.01	0.03	AATCAGTGGACTCCRAGGGGACTGAGACA	.	.	.	Other	3' UTR	.	.
AE1EX20	1213	A	0.64	T	0.36	0.46	ATTTGAGAGCCATTWTCCTCAACTCCATC	.	.	.	Other	3' UTR	.	.
AE1EX20	1342	T	0.94	C	0.06	0.12	AAAAATACAAAAATYAGCTGGGTGTCTCG	.	.	.	Other	3' UTR	.	.
AE1EX20	1628	G	0.95	C	0.05	0.10	CCCAGGAGGTGGAGSTTGCAGTGAGCCAA	.	.	.	Other	3' UTR	.	.
AE1EX20	1679	A	0.68	G	0.32	0.44	CTGGGCAACAGAGCRAGACCCTGTCTCAA	.	.	.	Other	3' UTR	.	.
AE1EX20	379	G	0.97	A	0.03	0.06	TCACTGGGGATCCCRTGCTGGAAGACTTA	.	.	.	Other	3' UTR	.	.
AE1EX20	418	C	0.99	A	0.01	0.03	CTCCCTCTTCCCAGMACAGGCAGGGGTAG	.	.	.	Other	3' UTR	.	.
AE1EX20	991	G	0.99	A	0.01	0.02	TTACTGAGGGCCCCRGAATCAGTGGACTC	.	.	.	Other	Intron	.	.
AE1EX4	17	C	0.98	T	0.03	0.05	CAATACTAACCGACYTCTGGTTTTCAGCT	.	.	.	Other	Asp	Ala	Ala
AE1EX4	36	A	0.91	C	0.09	0.16	GTTTTCAGCTCACGMCACCGAGGCAACAG	GAC	GCC	.	Nonsynonymous	Asp	Glu	Glu
AE1EX4	89	A	0.78	G	0.23	0.35	ACCCGGGTACCCACRAGGTGAGGACCCCA	AAG	GAG	.	Nonsynonymous	Lys	Ser	Ser
AE1EX5	197	A	0.97	T	0.03	0.06	CTAGAGCTGCGTAGWGTCTTCACCAAGGG	AGA	AGT	.	Nonsynonymous	Arg	Arg	Arg
AE1EX8	35	T	0.99	C	0.01	0.03	TTCCCACAGGGAGAYGGGGGCACAGAAGG	GAT	GAC	.	Synonymous	Asp	Asp	Asp

AGTEX2	181	C	0.99	T	0.01	0.03	AGAGTACCTGTGAGYAGCTGGCAAAGGCC	CAG	TAG	Nonsynonymous	Gln	Ala	STOP
AGTEX2	354	C	0.99	T	0.01	0.03	GTCGGGATGCTGGCYAACTTCTTGGGCTT	GCC	GCT	Synonymous	Ala	Ala	Ala
AGTEX2	755	T		G			GGACTTCACAGAACKGGATTGTTGCTGCTG	CTG	CGG	Nonsynonymous	Leu	Leu	Arg
AGTEX5	258	C	0.96	T	0.04	0.08	TGGCAAGGCCTCTGYCCCTGGCCTTTGAG	.	.	Other	3' UTR	3' UTR	.
AGTEX5	376	C	0.97	G	0.03	0.06	AGCTGGAAAGCAGCSGTTTCTCCTTGGTC	.	.	Other	3' UTR	3' UTR	.
AGTEX5	385	T	0.97	C	0.03	0.06	GCAGCCGTTTCTCCYTGGTCTAAGTGTGC	.	.	Other	3' UTR	3' UTR	.
AGTEX5	641	T	0.93	G	0.07	0.13	GCCTTCGGTTTGTAKTTAGTGTCTTGAAT	.	.	Other	3' UTR	3' UTR	.
AGTEXP1	101	G	0.99	C	0.01	0.03	CTGGCTGTGCTATTSTTGGTGTTTAACAG	.	.	Other	Promoter	Promoter	.
AGTEXP2	160	G	0.99	A	0.01	0.03	GGAACCTTGGCCCCRACTCCTGCAAACTT			Other	Promoter	Promoter	
AGTEXP2	35	G	0.97	A	0.03	0.06	CCCTCTGCACCTCCRGCCTGCATGTCCCT	.	.	Other	Promoter	Promoter	.
AGTEXP3	158	A	0.71	G	0.29	0.41	CTCGTGACCCGGCCRGGGGAAGAAGCTGC	.	.	Other	Promoter	Promoter	.
AGTEXP3	173	C	0.96	T	0.04	0.08	GGGGAAGAAGCTGCYGTTGTTCTGGGTAC	.	.	Other	Promoter	Promoter	.
ALDREDEX1	162	A	0.86	T	0.14	0.23	GCGCCAAGATGCCCWTCCTGGGGTTGGGT	ATC	TTC	Nonsynonymous	Ile	Phe	Phe
ALDREDEX1	71	C	0.41	G	0.59	0.48	AAAGGTACGCGCCGSGGCCAAGGCCGCAC	.	.	Other	Intron	Promoter	.
ALDREDEX10	150	T	0.91	G	0.09	0.16	TTGCAAATGTAGTAKGGCCTGTGTCACTC	.	.	Other	3' UTR	3' UTR	.
ALDREDEX2	180	C	0.94	G	0.06	0.11	TGAAGCGTGAGGAGSTCTTCATCGTCAGC	CTC	GTC	Nonsynonymous	Leu	Val	Val
ALDREDEX2	204	T	0.95	G	0.05	0.10	TCAGCAAGGTATCGKTCCGCGGTGGGGCT	.	.	Other	Intron	Intron	.
ALDREDEX2	88	A	0.98	T	0.03	0.05	CGTCGGGTACCGCCWCATCGACTGTGCCC	CAC	CTC	Nonsynonymous	His	Leu	Leu
ALDREDEX3	28	A	0.95	T	0.05	0.10	CCTCTCGCTGGCTTWGCTGTGGTGCACGT	.	.	Other	Intron	Intron	.
ALDREDEX4	101	G	0.98	A	0.03	0.05	AACATTCTGGACACRTGGGCGGTAAGACA	ACG	ACA	Synonymous	Thr	Thr	Thr
ALDREDEX6	87	G	0.94	A	0.06	0.11	ACTGCCAGTCCAAARGCATCGTGGTGACC	GGC	AGC	Nonsynonymous	Gly	Ser	Ser
ALDREDEX9	67	C	0.99	T	0.01	0.02	CCAGGATATGACCAYCTTACTCAGCTACA	ACC	ATC	Nonsynonymous	Thr	Ile	Ile
ANPEX1	232	G	0.99	A	0.01	0.03	CCATGTACAATGCCRTGTCCAACGCAGAC	GTG	ATG	Nonsynonymous	Val	Met	Met
ANPEX1	297	C	0.97	T	0.03	0.06	TAGGGCCAGGAAAGYGGGTGCAGTCTGGG	.	.	Other	Intron	Intron	.
ANPEX3	106	G	0.97	T	0.03	0.06	TCCTGTCCCCTGGGKTCTCTGCTGCATTT	.	.	Other	3' UTR	3' UTR	.
ANPEX3	127	T	0.91	C	0.09	0.16	CTGCATTTGTGTCAYCTTGTTGCCATGGA	.	.	Other	3' UTR	3' UTR	.
APOA1	101	C	0.76	T	0.24	0.36	GCCTTGCCCCAGGCYGGGCCTCTGGGTAC	.	.	Other	Promoter	Promoter	.
APOA1	1016	A	0.76	C	0.24	0.36	CGTAACTGGGCACCMGTCCCAGCTCTGTC	.	.	Other	Intron	Intron	.
APOA1	1162	G	0.94	C	0.06	0.12	AGGTGTCACCCAGGSCTCACCCCTGATAG	.	.	Other	Intron	Intron	.
APOA1	1163	C	0.93	T	0.08	0.14	GGTGTCACCCAGGGYTCACCCCTGATAGG	.	.	Other	Intron	Intron	.
APOA1	1401	G	0.99	C	0.01	0.02	TGCAGCCCTACCTGSACGACTTCCAGAAG	GAC	CAC	Nonsynonymous	Asp	His	His

APOA1	1576	G	0.98	C	0.02	0.04	TGTGGACGCGCTGCSCACGCATCTGGCCC	CGC	CCC	Nonsynonymous	Arg	Pro
APOA1	1643	G	0.98	A	0.02	0.04	CTTGAGGCTCTCAARGAGAACGGCGCGGC	AAG	AAA	Synonymous	Lys	Lys
APOA1	1757	C	0.94	G	0.06	0.11	CAAGGCCTGCTGCCSGTGCTGGAGAGCTT	CCC	CCG	Synonymous	Pro	Pro
APOA1	2007	T	0.64	A	0.36	0.46	CTCCGTGCCCAGACWGGACGTCTTAGGGC	.	.	Other	3' UTR	.
APOA1	334	T	0.69	C	0.31	0.43	AACCATCGGGGGGCYTTCTCCCTAAATCC	.	.	Other	Intron	.
APOA1	620	C	0.92	T	0.08	0.14	TTTGAAGGCTCCGCYTTGGGAAAACAGCT	GCC	GCT	Synonymous	Ala	Ala
APOA1	771	C	0.96	T	0.04	0.07	CTGGATGGAGAAACYGGAATGGATCTCCA	.	.	Other	Intron	.
APOA1	840	G	0.99	A	0.01	0.02	GGGCTGCCCGATGCRTGATCACAGAGCCA	.	.	Other	Intron	.
APOA2	1334	T	0.99	A	0.01	0.03	AGATTAGGCTTAAAWTGCAGAGAAAAAGT	.	.	Other	Intron	.
APOA2	1412	G	0.82	C	0.18	0.29	AAGAACTGGGCCTTSAATTTCAGTCTCTA	.	.	Other	Intron	.
APOA2	1414	A	0.95	T	0.05	0.10	GAACTGGGCCTTGAWTTTCAGTCTCTAGA	.	.	Other	Intron	.
APOA2	1459	C	0.99	T	0.01	0.03	AGCAAAGGTCTTGAYTCTATTCCTACCTA	.	.	Other	Intron	.
APOA2	1672	C	0.94	T	0.06	0.11	AGGCTGGAACGGAAYTGGTTAACTTCTTG	CTG	TTG	Synonymous	Leu	Leu
APOA2	249	T	0.55	C	0.45	0.50	TGCTTCCTGTTGCAYTCAAGTCCAAGGAC	.	.	Other	Promoter	.
APOA2	547	A	0.99	C	0.01	0.01	GACGCTGGCTAGGTMAGATAAGGAGGCAA	.	.	Other	Intron	.
APOA4	1228	A	0.75	G	0.25	0.38	GACCAGGTGGCCACRGTGATGTGGGACTA	ACA	ACG	Synonymous	Thr	Thr
APOA4	1338	T	0.03	C	0.97	0.06	GGGACTACAGTGTGYGGTGGTGACGGGGA	.	.	Other	Intron	.
APOA4	1479	C	0.98	T	0.03	0.05	CCACATATGTAAACYGGAAGTTTGGACCG	.	.	Other	Intron	.
APOA4	1529	T	0.86	C	0.14	0.24	TTGCTTTGACGTTCYAGAGTTTGACAAAT	.	.	Other	Intron	.
APOA4	1597	T	0.59	C	0.41	0.48	GGAGGAAAATGTCAYGTGAGCTGATTTCT	.	.	Other	Intron	.
APOA4	1617	G	0.99	A	0.01	0.02	CTGATTTCTAATACRTTTCAGAAAGACAG	.	.	Other	Intron	.
APOA4	1879	C	0.94	G	0.06	0.11	GATTCTGAGACAAASTATGTGGGAGATCC	.	.	Other	Intron	.
APOA4	1961	G	0.96	A	0.04	0.07	CTGCACCACCATAGRGAGGGTGAACTCGG	.	.	Other	Intron	.
APOA4	1998	T	0.63	C	0.37	0.47	AGCACTCACCTGTCYTAGCACGTGTGCAT	.	.	Other	Intron	.
APOA4	2134	C	0.73	T	0.28	0.40	GAAGTGAACACTTAYGCAGGTGACCTGCA	TAC	TAT	Synonymous	Tyr	Tyr
APOA4	2138	G	0.99	A	0.01	0.02	TGAACACTTACGCARGTGACCTGCAGAAG	GGT	AGT	Nonsynonymous	Gly	Ser
APOA4	2140	T	0.94	C	0.06	0.12	AACACTTACGCAGGYGACCTGCAGAAGAA	GGT	GGC	Synonymous	Gly	Gly
APOA4	2358	A	0.89	G	0.11	0.20	GCGCACCCAGGTCARCACGCAGGCCGAGC	AAC	AGC	Nonsynonymous	Asn	Ser
APOA4	2698	C	0.95	T	0.05	0.10	ATCTCGGCCAGTGCYGAGGAGCTGCGGCA	GCC	GCT	Synonymous	Ala	Ala
APOA4	2764	C	0.92	T	0.08	0.15	CTGAGGGGCAACACYGAGGGGCTGCAGAA	ACC	ACT	Synonymous	Thr	Thr
APOA4	2806	G	0.99	A	0.01	0.02	CTGGGTGGGCACCTRGACCAGCAGGTGGA	CTG	CTA	Synonymous	Leu	Leu

APOA4	2837	G	0.98	C	0.02	0.04	AGTTCCGACGCCCGGGTGGAGCCCTACGGG	GTG	CTG	Nonsynonymous	Val	Leu
APOA4	2926	G	0.81	T	0.19	0.30	CATGCGGGGGACGTKGAAGGCCACTTGAG	GTG	GTT	Synonymous	Val	Val
APOA4	3058	T	0.16	G	0.84	0.26	CAGCAGGAACAGCAKCAGGAGCAGCAGCA	CAT	CAG	Nonsynonymous	His	Gln
APOA4	350	G	0.88	A	0.12	0.21	GCCAGCAGGGCCTCRAGGCATCAGTCCCG	.	.	Other	Promoter	.
APOA4	637	G	0.96	C	0.04	0.08	TGGCGATAGGGAGASAGTTTAAATGTCTG	.	.	Other	Promoter	.
APOA4	687	G	0.96	A	0.04	0.07	GTTCCCACTGCAGCRCAGGTGAGCTCTCC	.	.	Other	Promoter	.
APOC1EX1	1020	G	0.93	T	0.07	0.13	TTGTATTTTCAGTAKAGACAGGGTTTCAC	.	.	Other	Intron	.
APOC1EX1	1044	G	0.95	A	0.05	0.10	TTCACCGTGGTCTCRATCTCCTGACTTTG	.	.	Other	Intron	.
APOC1EX1	1057	T	0.64	C	0.36	0.46	CGATCTCCTGACTTYGTGATCCGCCTGCC	.	.	Other	Intron	.
APOC1EX1	1111	C	0.89	T	0.11	0.20	CAGGCGTGAGCCACYGCGTCCGGCCATTC	.	.	Other	Intron	.
APOC1EX1	1376	G	0.57	T	0.43	0.49	GCACGCGCCCTGTAGKCCCAGCTACTCGGG	.	.	Other	Intron	.
APOC1EX1	1411	C	0.99	G	0.01	0.02	AGGCAGGAGAATCASTTGAACCCGGGAGG	.	.	Other	Intron	.
APOC1EX1	432	G	0.97	A	0.03	0.06	AGGCTCTTCCTGTCRCTCCCGGTCCTGGT	TCG	TCA	Synonymous	Ser	Ser
APOC1EX1	462	C	0.61	G	0.39	0.47	GTGGTTCTGTCGATSCTCTTGGAAGGTAA	ATC	ATG	Nonsynonymous	Ile	Met
APOC1EX1	496	G	0.01	C	0.99	0.02	GGATGGGAGAATTGSGGAGTTTGGAGATT	.	.	Other	Intron	.
APOC1EX1	713	C	0.99	T	0.01	0.02	ACCTCTGGGATTGGYTGTCCTGCTTCGAC	.	.	Other	Intron	.
APOC2	1084	T	0.91	G	0.09	0.17	TCTGAGGACTCAAGKGCCAAGATGGAGGG	.	.	Other	3' UTR	.
APOC2	126	C	0.99	T	0.01	0.02	CAGGTCTCTGGACAYTATGGGCACACGAC	.	.	Other	5' UTR	.
APOC2	13	T	0.34	A	0.66	0.45	CTGGGACACCGAGCWCACACAGAGGCAGGA	.	.	Other	Promoter	.
APOC2	472	G	0.99	A	0.01	0.02	CCCAGAACCTGTACRAGAAGACATACCTG	GAG	AAG	Nonsynonymous	Glu	Lys
APOC2	553	G	0.99	A	0.01	0.02	TGGCCCATACCACCRACTGCATCCAGGAC	.	.	Other	Intron	.
APOC2	725	T	0.19	C	0.81	0.31	CCCAGGAGTCCAGGYCCCCAGACCCTCCT	.	.	Other	Intron	.
APOC2	804	A	0.97	T	0.03	0.06	TGTGCTTTCTCCCCWGGGACTTGTACAGC	.	.	Other	Intron	.
APOC2	819	A	0.82	C	0.18	0.30	GGGACTTGTACAGCMAAAGCACAGCAGCC	AAA	CAA	Nonsynonymous	Lys	Gln
APOC3	1148	T	0.95	A	0.05	0.10	CTGGGGACTAAGAAWGTTTATGAACACCT	.	.	Other	Intron	.
APOC3	1322	G	0.71	A	0.29	0.41	CACGGGCTTGAATTRGGTCAGGTGGGGCC	.	.	Other	Intron	.
APOC3	1468	A	0.97	C	0.03	0.06	ATACGCCTGAGCTCMGCCTCCTGTCAGAT	.	.	Other	Intron	.
APOC3	1519	A	0.95	G	0.05	0.10	GGAGTGTGAACCCTRTTGTGAACTGCACA	.	.	Other	Intron	.
APOC3	1637	T	0.96	A	0.04	0.07	GGCCCATGGAAAAAWTGTCCACCACAAAA	.	.	Other	Intron	.
APOC3	1722	A	0.84	G	0.16	0.27	AGGAAAATGGGGCCRGGCGCAGTGGCTCG	.	.	Other	Intron	.
APOC3	1728	A	0.73	G	0.27	0.40	ATGGGGCCAGGCGCRGTGGCTCATGCCTG	.	.	Other	Intron	.

APOC3	1736	A	0.85	G	0 15	0 26	AGGCGCAGTGGCTCRTGCCTGTAATCCCA	.	.	.	Other	Intron	.
APOC3	1774	A	0.76	C	0.24	0.36	GAGGCCGAGGCAGGMGGATCCCCTGAGGT	.	.	.	Other	Intron	.
APOC3	1817	T	0.69	C	0.31	0.43	CAACCTGGCCAACAYGGTGAAACCCCATC	.	.	.	Other	Intron	.
APOC3	1931	C	0.98	T	0.02	0.04	TTGAACCCGGGAGAYGGAGGTTGCAGTGA	.	.	.	Other	Intron	.
APOC3	1975	G	0.99	A	0.01	0.03	CTGCACTCCAGCCTRGGTGACAGAGGGAG	.	.	.	Other	Intron	.
APOC3	2221	G	0.96	A	0.04	0.08	AGGGCTAAAACGGCRCGGCCCTAGGACTG	.	.	.	Other	Intron	.
APOC3	2535	G	0.81	A	0.19	0.30	GCGTGCTTCATGTARCCCTGCATGAAGCT	GGC	GGT	Synonymous	Gly	Gly	Gly
APOC3	2854	C	0.70	T	0.30	0.42	CCCTGGGGAGGTGGYGTGGCCCCTAAGGT	.	.	.	Other	Promoter	.
APOC3	429	A	0.69	C	0.31	0.43	GCAACCTACAGGGGMAGCCCTGGAGATTG	.	.	.	Other	3' UTR	.
APOC3	460	G	0.99	C	0.01	0.03	GGACCCAAGGAGCTSGCAGGATGGATAGG	.	.	.	Other	3' UTR	.
APOC3	636	G	0.96	A	0.04	0.07	TAAATCAGTCAGGGRAAGCAACAGAGCAG	.	.	.	Other	Intron	.
APOC3	954	A	0.89	G	0.11	0.19	GTGCAAACAGCACCRCCTGGAGTTGCACA	.	.	.	Other	Intron	.
APOC4	1150	T	0.39	C	0.61	0.47	AAGTGCTAGGATTAYAGGCGTGAGCCACT	.	.	.	Other	Intron	.
APOC4	1246	A	0.33	C	0.67	0.44	AGGCTGGTCTTGAAMTCCTGACCTCAGGT	.	.	.	Other	Intron	.
APOC4	1281	C	0.91	T	0.09	0.16	CCCGCCTTGGCCTCYCAAAGTGCTGGGAT	.	.	.	Other	Intron	.
APOC4	1287	T	0.95	C	0.05	0.10	TTGGCCTCCCAAAGYGCTGGGATTACAGG	.	.	.	Other	Intron	.
APOC4	1313	A	0.42	G	0.58	0.49	AGGCATGAGCCACCRCGCCCGGCCATGTA	.	.	.	Other	Intron	.
APOC4	1406	G	0.87	A	0.13	0.22	ACAGGGCCAGGCACRGTGGCTCATGCCTG	.	.	.	Other	Intron	.
APOC4	1446	G	0.91	A	0.09	0.16	CTTTCGGAGGCCGARGCGGGTGGATCGCA	.	.	.	Other	Intron	.
APOC4	1587	C	0.29	A	0.71	0.41	CGGGAGGCTGAGGCMGGAGAATCACTTGA	.	.	.	Other	Intron	.
APOC4	1782	G	0.96	C	0.04	0.07	ATAACCCTGAGGTASATATTATTACCCCG	.	.	.	Other	Intron	.
APOC4	1794	C	0.94	T	0.06	0.11	TAGATATTATTACCYCGTTCTACAAAAGG	.	.	.	Other	Intron	.
APOC4	1842	G	0.98	A	0.03	0.05	CAGGATAAGTCACCRGCCAAGGCACACAG	.	.	.	Other	Intron	.
APOC4	1858	T	0.36	C	0.64	0.46	CCAAGGCACACAGCYAGCTACATGTGGCC	.	.	.	Other	Intron	.
APOC4	1875	C	0.96	T	0.04	0.07	CTACATGTGGCCCCYGCGTGACGGCTGGT	.	.	.	Other	Intron	.
APOC4	2206	A	0.92	G	0.08	0.15	TGAAGAGATGGCCCCRGCCCGGACGGGGTGG	.	.	.	Other	Intron	.
APOC4	2237	C	0.94	T	0.06	0.12	CACATCTGTAATCCYAGCATTTTGGGAGC	.	.	.	Other	Intron	.
APOC4	2276	T	0.65	C	0.35	0.46	TGGATCACTTGAGGYCAGGAGTTCGAGGC	.	.	.	Other	Intron	.
APOC4	2345	A	0.74	G	0.26	0.38	ATTAGCCGGGCATGRTGGCAGATGCCTGT	.	.	.	Other	Intron	.
APOC4	2366	T	0.51	A	0.49	0.50	ATGCCTGTAATCCCWGCTACTCGGGAGGC	TGG	TGA	Nonsynonymous	Trp	Stop	.
APOC4	2767	G	0.99	A	0.01	0.02	AAGATGAGTCGCTGRAGCCTGGTGAGGGG	.	.	.	Other	Intron	.

APOC4	3027	G	0.98	A	0.03	0.05	TCACAGAGAGGAGCRGATAAATGGGGCAG	.	.	Other	Intron	.	
APOC4	3078	G	0.96	C	0.04	0.08	GCCTCCACTGTGATSTCCTCTCTCCTGTA	.	.	Other	Intron	.	
APOC4	3162	T	0.51	G	0.49	0.50	GGACCTGGGTCCCGCKCACCAAGGCCTGGT	CTC	CGC	Nonsynonymous	Leu	Arg	
APOC4	3252	A	0.91	T	0.09	0.17	TGGGGACAAGGACCWGGGTTAAAATGTTC	CAG	CTG	Nonsynonymous	Gln	Leu	
APOC4	483	T	0.95	G	0.05	0.10	CTGAGAGTGAAGTGKGAATGTCACATTGG	.	.	Other	Intron	.	
APOC4	931	A	0.97	G	0.03	0.06	CCAGGCTGGAGTGCRGTGGCGTGATCTTG	.	.	Other	Intron	.	
APOC4	968	C	0.76	T	0.24	0.36	CAAGCTCCGCCTCCYGGGTTCACGCCATT	.	.	Other	Intron	.	
APOER2EX1	454	G	0.98	C	0.02	0.04	CGCGGCAAGGACTCSGAGGGCTGAGACGC	.	.	Other	5' UTR	.	
APOER2EX12	68	A	0.96	C	0.04	0.07	ACCAACTGTCCAGCMTTGACTTCAGTCGA	ATT	CTT	Nonsynonymous	Ile	Leu	
APOER2EX13	55	G	0.99	C	0.01	0.02	CGAGGCCATTTTCASTGCAAATCGGCTCA	AGT	ACT	Nonsynonymous	Ser	Thr	
APOER2EX14	162	G	0.98	A	0.03	0.05	GAAGAGGTGCTACCRAGGTAAGCAGACCT	CGA	CAA	Nonsynonymous	Arg	Gln	
APOER2EX17	55	A	0.98	G	0.03	0.05	TACCTGATCTGGAGRAACTGGAAGCGGAA	AGA	AGG	Synonymous	Arg	Arg	
APOER2EX19	1005	G	0.52	C	0.48	0.50	AGAGTGCTCAGAAASTCAAGATAGGATAT	.	.	Other	3' UTR	.	
APOER2EX19	1060	T	0.96	C	0.04	0.07	TAAAGTTCAGCTCTYTGAGTAACTTCTTC	.	.	Other	3' UTR	.	
APOER2EX19	1149	A	0.98	T	0.03	0.05	TGCCATCCTTACAGWGCTAAGTGGAGACG	.	.	Other	3' UTR	.	
APOER2EX19	13	G	0.51	A	0.49	0.50	GTTGTCTCCCCAGCRAGTGGCATTAAGCC	CGA	CAA	Nonsynonymous	Arg	Gln	
APOER2EX19	602	A	0.93	G	0.07	0.13	TTTAGAGAAGTGAGRGTATTTATTTTTGG	.	.	Other	3' UTR	.	
APOER2EX19	931	A	0.99	C	0.01	0.02	CCATGGCTGCTGTGMCTCCTACCAGGGCT	.	.	Other	3' UTR	.	
APOER2EX9	116	G	0.99	A	0.01	0.03	TGCTCAAGAATGTCRTGGCACTAGATGTG	GTG	ATG	Nonsynonymous	Val	Met	
APOER2EX9	157	G	0.99	C	0.01	0.02	AATCGCATCTACTGSTGTGACCTCTCCTA	TGG	TGC	Nonsynonymous	Trp	Cys	
AT1EX5	1158	A	0.95	G	0.05	0.10	TGAGGTTGAGTGACRTGTTCGAAACCTGT	.	.	Other	3' UTR	.	
AT1EX5	1226	T	0.92	G	0.08	0.15	TCCTCTGCAGCACTKCACTACCAAATGAG	.	.	Other	3' UTR	.	
AT1EX5	1242	A	0.53	C	0.47	0.50	ACTACCAAATGAGCMTTAGCTACTTTTCA	.	.	Other	3' UTR	.	
AT1EX5	1249	A	0.99	G	0.01	0.03	AATGAGCATTAGCTRCTTTTCAGAATTGA	.	.	Other	3' UTR	.	
AT1EX5	1473	G	0.91	A	0.09	0.17	CCTGCTTTTGTCCTRTTATTTTTTATTTC	.	.	Other	3' UTR	.	
AT2EX3	1355	T	0.39	G	0.61	0.47	GTTTGTACAAGATTKTCATTGGTGAGACA	.	.	Other	3' UTR	.	
AT2EX3	1361	G	0.69	A	0.31	0.43	ACAAGATTTTCATTRGTGAGACATATTTA	.	.	Other	3' UTR	.	
AT2EX3	562	T	0.99	C	0.01	0.03	TATATAGTTCCCCTYGTTTGGTGTATGGC	CTT	CTC	Synonymous	Leu	Leu	
AT2EX3	807	G	0.94	A	0.06	0.12	CTATGGGAAGAACARGATAACCCGTGACC	AGG	AAG	Nonsynonymous	Arg	Lys	
AT2EX3	844	T	0.93	C	0.07	0.13	AAGATGGCAGCTGCYGTTGTTCTGGCCTT	GCT	GCC	Synonymous	Ala	Ala	
AVPEX2	154	C	0.96	T	0.04	0.08	GGAGAACTACCTGCYGTCGCCCTGCCAGT	CCG	CTG	Nonsynonymous	Pro	Leu	

AVPR2EX1	114	A	0.97	T	0.03	0.06	TCATGGCGTCCACCWCTTCCGGTAAGGCT	ACT	TCT	Nonsynonymous	Thr	Ser
AVPR2EX2	109	G	0.98	A	0.02	0.04	ACCCGGGACCCGCTRCTAGCCCGGGCGGA	CTG	CTA	Synonymous	Leu	Leu
AVPR2EX2	129	C	0.85	T	0.15	0.25	CCGGGCGGAGCTGGYGCTGCTCTCCATAG	GCG	GTG	Nonsynonymous	Ala	Val
AVPR2EX2	184	G	0.94	T	0.06	0.11	GGCCTGGTGCTGGCKGCCCTAGCTCGGCG	GCG	GCT	Synonymous	Ala	Ala
AVPR2EX2	444	C	0.87	T	0.13	0.23	CCGTCCCATGCTGGYGTACCGCCATGGAA	GCG	GTG	Nonsynonymous	Ala	Val
AVPR2EX3	112	C	0.95	T	0.05	0.10	TCTTTCAGCAGCAGYGTGTCCTCAGAGCT	AGC	AGT	Synonymous	Ser	Ser
AVPR2EX3	232	G	0.95	A	0.05	0.10	AAGGACACTTCATCRTGAGGAGCTGTTGG	TCG	TCA	Synonymous	Ser	Ser
AVPR2EX3	252	T	0.97	C	0.03	0.06	AGCTGTTGGGTGTCYTGCCTCTAGAGGCT	.	.	Other	3' UTR	.
AVPR2EX3	46	A	0.50	G	0.50	0.50	GCGCCCTTTGTGCTRCTCATGTTGCTGGC	CTA	CTG	Synonymous	Leu	Leu
BIR	1069	C	0.98	T	0.03	0.05	CAGGACTGGCTGGAYGCACAGCTCTAGGG	.	.	Other	3' UTR	.
BIR	1142	G	0.67	A	0.33	0.44	GGTGAGCCAGTCCTRAATTGGGTTGGGAG	.	.	Other	3' UTR	.
BIR	1185	G	0.98	T	0.03	0.05	ATAACCCAGTACAGKTTCCTGCTGAGGCC	.	.	Other	3' UTR	.
BIR	1265	G	0.95	A	0.05	0.10	GGAGGCTGAGCTGARGCTGGCCCAGCCTC	.	.	Other	3' UTR	.
BIR	1295	C	0.24	T	0.76	0.37	CACCAGGCCCTGGCVGGGCTACATACCAC	.	.	Other	3' UTR	.
BIR	1441	T	0.99	C	0.01	0.02	AGGGGCCCGCGGGCYGAGGCGAGGGTCAG	TCA	TCG	Synonymous	Ser	Ser
BIR	1521	C	0.26	T	0.74	0.38	TGTGGGCACTTTGAYGGTGTTGCCAAACT	GTC	ATC	Nonsynonymous	Val	Ile
BIR	1729	G	0.99	C	0.01	0.03	GGTGCCAGGTCGTASAGTGGGCTGTTGGC	CTC	CTG	Synonymous	Leu	Leu
BIR	1946	C	0.99	T	0.01	0.02	GCATCAAGCAGAGGYGGCCGTGGCCGCAGG	CGC	CAC	Nonsynonymous	Arg	His
BIR	1960	G	0.75	A	0.25	0.38	CGGCCGTGGCGCAGRGCGATCACCGCATG	GCC	GCT	Synonymous	Ala	Ala
BIR	2463	T	0.22	C	0.78	0.34	ACGGTACCTGGGCTYGGCAGGGTCCTCTG	AAG	GAG	Nonsynonymous	Lys	Glu
BIR	2664	T	0.97	C	0.03	0.06	TGTGCTGGCCTCACYTCTGAGATAACTCC	.	.	Other	5' UTR	.
BIR	2894	T	0.99	G	0.01	0.03	TGGTGGTGCGCACCKGTAATCCCACCTAC	.	.	Other	Promoter	.
BIR	2954	G	0.97	C	0.03	0.06	CCCGAGAGGCGGAGSTTGCAGTGAGCCAA	.	.	Other	Promoter	.
BIR	3174	C	0.70	T	0.30	0.42	TCCCGCTAAGAGCCYTTCTCCCCGCCCAG	.	.	Other	Promoter	.
BIR	369	G	0.97	A	0.03	0.06	CAACACTGCTCCAARGGTCCAGGCACGGG	.	.	Other	3' UTR	.
BIR	510	T	0.99	C	0.01	0.02	CCTTCTGGACAAAGYGAGTGGCAGCCACT	.	.	Other	3' UTR	.
BIR	657	T	0.92	A	0.08	0.14	CACAGAGCCCTCACWGCACGAGGCCGATG	.	.	Other	3' UTR	.
BIR	981	G	0.98	A	0.03	0.05	TTGGAGCCACAGACRCAAAGCAGCAGCCC	.	.	Other	3' UTR	.
BKRB2EX1	55	T	0.77	G	0.23	0.35	GGTGGGGACGGTGGKGACGGTGGGGACAT	.	.	Other	5' UTR	.
BKRB2EX3	1513	T	0.93	C	0.07	0.13	ATCTCCAGGAGAACYGCCATCCAGCTTTG	.	.	Other	3' UTR	.
BKRB2EX3	1833	G	0.95	A	0.05	0.10	ACTCAAGTGGGAACRACTGGGCACTGCCA	.	.	Other	3' UTR	.

BKRB2EX3	747	G	0.93	A	0.07	0.13	AAGGAGATCCAGACRGAGAGGAGGGCCAC	ACG	ACA	Synonymous	Thr	Thr
BNPEX1	343	G	0.99	T	0.01	0.02	TTTCCTGGGAGGTCKTTCCCACCCGCTGG	CGT	CTT	Nonsynonymous	Arg	Leu
BNPEX2	15	C	0.97	G	0.03	0.07	TGAGGCTTGGACGCSCCCATTCATTGCAG	.	.	Other	Intron	.
BNPEX2	174	A	0.99	T	0.01	0.02	GTGGGCACCGCAAAWTGGTCCTCTACACC	ATG	TTG	Nonsynonymous	Met	Leu
BNPEX2	37	G	0.97	A	0.03	0.06	ATTGCAGGAGCAGCRCAACCATTTGCAGG	CGC	CAC	Nonsynonymous	Arg	His
BRS3EX1	424	G	0.95	A	0.05	0.10	AGAACTGAAGCAAARGAGTATCTGGATGT	.	.	Other	Promoter	.
BRS3EX1	730	A	0.97	C	0.03	0.06	GTGCCATCTATATTMCTTATGCTGTGATC	ACT	CCT	Nonsynonymous	Thr	Pro
BRS3EX1	879	A	0.95	T	0.05	0.10	CTAACTTGTGTGCCWGTGGATGCAACTCA	CCA	CCT	Synonymous	Pro	Pro
BRS3EX2	144	T	0.94	A	0.06	0.11	GCTCTACCTGAGGCWATATTTTCAAATGT	GCT	GCA	Synonymous	Ala	Ala
BRS3EX2	80	T	0.98	A	0.02	0.04	CTCCAATGCCATCCWGAAGACTTGTGTAA	CTG	CAG	Nonsynonymous	Leu	Gln
BRS3EX3	173	T	0.94	C	0.06	0.12	GCCATGCATTTCATYTTCACCATTTTCTC	ATT	ATC	Synonymous	Ile	Ile
CALCGRPEX1+2	1063	T	0.98	G	0.02	0.05	CCCCAGTCACAGGCKCTGGGAGCAAAGAG	.	.	Other	5' UTR	.
CALCGRPEX1+2	940	G	0.86	A	0.14	0.24	GTGCGATCAGGGACRGCGTCTGGAGCCCA	.	.	Other	5' UTR	.
CALCGRPEX3	112	G	0.92	A	0.08	0.15	CTGCACTGGTGCAGRACTATGTGCAGATG	GAC	AAC	Nonsynonymous	Asp	Asn
CALCGRPEX3	120	G	0.99	T	0.01	0.02	GTGCAGGACTATGTKCAGATGAAGGCCAG	GTG	GTT	Synonymous	Val	Val
CALCGRPEX4	30	C	0.91	A	0.09	0.16	TGTTTTCCCTGCAGMCTGGACAGCCCCAG	AGC	AGA	Nonsynonymous	Ser	Arg
CALCGRPEX5	309	A	0.59	T	0.41	0.48	ATGTGGTTTTAAAAWATCCATAAGGGAAG	.	.	Other	3' UTR	.
CALCGRPEX5	433	C	0.78	T	0.22	0.34	CAGACCAAGAAATAYAGATCCTGTTTATT	.	.	Other	3' UTR	.
CALCGRPEX5	719	G	0.91	A	0.09	0.16	AAAGAGCAAGTGAGRTAATAGATGTTAAG	.	.	Other	3' UTR	.
CHYEX1	158	T	0.86	A	0.14	0.24	TTGCCTTCTGGGAGWTATAAAACCCAAGA	.	.	Other	5' UTR	.
CHYEX1	65	T	0.70	C	0.30	0.42	TCTAGGGGAACTTCYGATCAGAAACAGCC	.	.	Other	5' UTR	.
CHYEX2	107	G	0.95	C	0.05	0.09	TTGTAACTTCCAACSGTCCCTCAAAATTT	GGT	CGT	Nonsynonymous	Gly	Arg
CHYEX2	168	A	0.92	G	0.08	0.14	GCTGACGGCTGCTCRTTGTGCAGGAAGGT	CAT	CGT	Nonsynonymous	His	Arg
CHYEX3	26	A	0.91	G	0.09	0.17	CCTTCTTCCTCACARCAGGTCTATAACAG	.	.	Other	Intron	.
CHYEX4	83	A	0.92	C	0.08	0.15	CTCCCCTTCCCATCMCAATTCAACTTTGT	TCA	TCC	Synonymous	Ser	Ser
CHYEX5	274	C	0.89	T	0.11	0.19	TCCCTCAGCCACAAYCCTAAGCCTCCAGA	.	.	Other	3' UTR	.
CLCNKBEX10	33	G	0.56	C	0.44	0.49	CTCTGGCCACCTTGSTTCTCGCCTCCATC	GTT	CTT	Nonsynonymous	Val	Leu
CLCNKBEX13	12	C	0.94	T	0.06	0.12	GGAGGAGCTGCTATYGGGCGCCTCTTTGG	ATC	ATT	Synonymous	Ile	Ile
CLCNKBEX15	64	C	0.94	T	0.06	0.11	ACTGGCCAAGGACAYGCCACTGGAGGAGG	ACG	ATG	Nonsynonymous	Thr	Met
CLCNKBEX15	68	A	0.34	G	0.66	0.45	GCCAAGGACACGCCRCTGGAGGAGGTGGT	CCA	CCG	Synonymous	Pro	Pro
CLCNKBEX18	51	C	0.96	T	0.04	0.08	CCTCTTTGTGACGTYGCGGGGCAGAGCTG	TCG	TGG	Nonsynonymous	Ser	Trp

CLCNKBEX3	34	A	0.94	C	0.06	0.11	GGGAGATTGGGGACMGCCACCTGCTCCGG	AGC	CGC	Nonsynonymous	Ser	Arg
CLCNKBEX3	96	G	0.93	A	0.07	0.13	GTCTCTTTCTCTTCRGGCTTCTCTCAGAG	TCG	TCA	Synonymous	Ser	Ser
CLCNKBEX4	19	G	0.35	C	0.65	0.46	CTGGAATCCCGGAGSTGAAGACCATGTTG	GTG	CTG	Nonsynonymous	Val	Leu
CLCNKBEX4	70	A	0.92	C	0.08	0.15	ACCTGGATATCAAGMACTTTGGGGCCAAA	AAC	CAC	Nonsynonymous	Asn	His
CLCNKBEX7	108	G	0.89	A	0.11	0.20	TTCCGGCTCCTGGCRGTCTTCAACAGCGA	GCG	GCA	Synonymous	Ala	Ala
CNPEX1	1018	C	0.91	A	0.09	0.16	GCAGCGCCAACTTTMTGCCTGTATGACTT	.	.	Other	5' UTR	.
CNPEX1	144	G	0.98	T	0.02	0.04	GCCTTCACGCCTGGKGACAGCCACTGCAC	.	.	Other	5' UTR	.
CNPEX1	1457	C	0.98	G	0.02	0.05	GCAGCACTGGGACCSTGCTCGCCCTGCAG	.	.	Other	5' UTR	.
CNPEX1	578	G	0.91	A	0.09	0.16	ATTGTTCCCACAGARGGAGTTCACCAGCG	.	.	Other	5' UTR	.
CNPEX1	592	G	0.94	A	0.06	0.11	GGGAGTTCACCAGCRGAGTCAGACCCCGG	.	.	Other	5' UTR	.
CNPEX2	1171	T	0.92	A	0.08	0.14	AACATCCCAGCCTCWGACATTGACAGTCA	.	.	Other	3' UTR	.
CNPEX2	139	G	0.96	A	0.04	0.08	GGACACCAAGTCGCRGGCAGCGTGGGCTC	CGG	CAG	Nonsynonymous	Arg	Gln
CNPEX2	357	A	0.95	G	0.05	0.10	CCCGCCGCCCAGCCRGCCTTCGGAGGCGC	.	.	Other	3' UTR	.
CNPEX2	41	T	0.98	C	0.02	0.03	GCTGCGGGCCGGCGGYCAGAAGAAGGGCGA	GGT	GGC	Synonymous	Gly	Gly
COX1	1063	A	0.99	G	0.01	0.02	TTTCCTGCAGCTGARATTTGACCCAGAGC	AAA	AGA	Nonsynonymous	Lys	Arg
COX1	1314	A	0.99	G	0.01	0.02	ACATGGACCACCACRTCCTGCATGTGGCT	ATC	GTC	Nonsynonymous	Ile	Val
COX1	1386	A	0.99	G	0.01	0.02	TCAATGAGTACCGCRAGAGGTTTGGCATG	AAG	GAG	Nonsynonymous	Lys	Glu
COX1	1428	G	0.98	A	0.02	0.03	CCTTCCAGGAGCTCRTAGGAGAGAAGGAG	GTA	ATA	Nonsynonymous	Val	Ile
COX1	1906	T	0.96	C	0.04	0.08	GGTGAGTGTTGGGGYTGACATTTAGAACT	.	.	Other	3' UTR	.
COX1	1948	T	0.99	C	0.01	0.02	ATTATCTGGAATAYGTGATTCTGTTTAT	.	.	Other	3' UTR	.
COX1	2037	T	0.99	G	0.01	0.02	GTCTGCCAGAATACKGGTTCTTAGTTGA	.	.	Other	3' UTR	.
COX1	310	G	0.99	A	0.01	0.02	TGCCACCTTCATCCRAGAGATGCTCATGC	CGA	CAA	Nonsynonymous	Arg	Gln
COX1	626	C	0.91	A	0.09	0.16	TTCAAAACTTCTGGMAAGATGGGTCCTGG	GGC	GGA	Synonymous	Gly	Gly
COX1	696	C	0.98	A	0.02	0.03	TTTATGGAGACAATMTGGAGCGTCAGTAT	CTG	ATG	Nonsynonymous	Leu	Met
COX1	938	T	0.98	C	0.02	0.04	GACCTGCTGAAGGCYGAGCACCCCACCTG	GCT	GCC	Synonymous	Ala	Ala
COX2EX1	186	C	0.84	G	0.16	0.27	CGATTTTCTCATTTSCGTGGGTAAAAAAC	.	.	Other	Promoter	.
COX2EX1	358	T	0.84	G	0.16	0.27	GCGACCAATTGTCAKACGACTTGCAGTGA	.	.	Other	Promoter	.
COX2EX10	156	T	0.94	C	0.06	0.12	AACCATGGTAGAAGYTGGAGCACCATTCT	GTT	GCT	Nonsynonymous	Val	Ala
COX2EX10	379	C	0.98	A	0.03	0.05	GCAAGTTCTTCCCGMTCCCGACTAGATGA	CGC	CGA	Synonymous	Arg	Arg
COX2EX10	866	T	0.51	C	0.49	0.50	AAAGTACTTTTGGTYATTTTTCTGTCATC	.	.	Other	3' UTR	.
COX2EX10	87	A	0.99	G	0.01	0.02	CATCGATGCTGTGGRGCTGTATCCTGCCC	GAG	GGG	Nonsynonymous	Glu	Gly

COX2EX10	937	G	0.83	A	0.17	0.28	ATTAGACATTACCARTAATTTCATGTCTA	.	.	Other	3'UTR	.	
COX2EX3	166	G	0.93	C	0.07	0.13	ATTATGAGTTATGTSTTGACATGTAAGTA	GTG	GTC	Synonymous	Val	Val	
COX2EX7	206	T	0.96	C	0.04	0.07	AACAGAGTATGCGAYGTGCTTAAACAGGA	GAT	GAC	Synonymous	Asp	Asp	
COX2EX8	268	T	0.95	C	0.05	0.10	ATATTGCTGGAACAYGGAATTACCCAGTT	CAT	CAC	Synonymous	His	His	
CYP11B1EX1	351	T	0.97	C	0.03	0.06	TGACGTGATCCCTCYCGAAGGCAAGGCAC	.	.	Other	Promoter	.	
CYP11B1EX1	525	C	0.99	G	0.01	0.03	AGGACAGTGCTGCCSTTTGAAGCCATGCC	CCC	CCG	Synonymous	Pro	Pro	
CYP11B1EX1	542	G	0.97	A	0.03	0.06	TGAAGCCATGCCCCRGCGTCCAGGCAACA	CGG	CAG	Nonsynonymous	Arg	Gln	
CYP11B1EX1	601	G	0.97	C	0.03	0.06	AGCAGGGTTATGAGSACCTGCACCTGGAA	GAC	CAC	Nonsynonymous	Asp	His	
CYP11B1EX2	184	C	0.99	T	0.01	0.03	GTGGCGTGTTCTTGTYGTAAGCGGCGAGC	CTG	TTG	Synonymous	Leu	Leu	
CYP11B1EX2	188	A	0.96	G	0.04	0.07	CGTGTTCTTGCTGTRAGCGGCGAGCTGAG	.	.	Other	Intron	.	
CYP11B1EX2	36	T	0.46	C	0.54	0.50	CCCCACAGGTACGAYTTGGGAGGAGCAGG	GAT	GAC	Synonymous	Asp	Asp	
CYP11B1EX2	78	C	0.96	T	0.04	0.08	ATGCTGCCGGAGGAYGTGGAGAAGCTGCA	GAC	GAT	Synonymous	Asp	Asp	
CYP11B1EX3	114	G	0.99	C	0.01	0.02	AGGTTCCTCCCCGATSGTGGATGCAGTGGC	ATG	ATC	Nonsynonymous	Met	Ile	
CYP11B1EX4	177	C	0.98	T	0.02	0.04	CCTGTCTCGCTGGAYCAGCCCCAAGGTGT	ACC	ATC	Nonsynonymous	Thr	Ile	
CYP11B1EX4	205	T	0.92	G	0.08	0.15	TGGAAGGAGCACTTKGAGGCCTGGGACTG	TTT	TTG	Nonsynonymous	Phe	Leu	
CYP11B1EX4	247	C	0.91	G	0.09	0.16	GGTGAGGCCAGGGASCCGGGCAGTGCTAT	.	.	Other	Intron	.	
CYP11B1EX5	103	G	0.97	A	0.03	0.06	ACCAGCATCGTGGCRGAGCTCCTGTTGAA	GCG	GCA	Synonymous	Ala	Ala	
CYP11B1EX5	107	C	0.84	G	0.16	0.26	GCATCGTGGCGGAGSTCCTGTTGAATGCG	CTC	GTC	Nonsynonymous	Leu	Val	
CYP11B1EX5	16	C	0.58	T	0.42	0.49	TGAGGGCTGCCTCCYGCTCCCCGGATAGG	.	.	Other	Intron	.	
CYP11B1EX5	55	T	0.97	C	0.03	0.06	ATCCAGAAAATCTAYCAGGAACTGGCCTT	TAT	TAC	Synonymous	Tyr	Tyr	
CYP11B1EX5	72	G	0.99	A	0.01	0.03	GGAACTGGCCTTCARCCGCCCTCAACAGT	AGC	AAC	Nonsynonymous	Ser	Asn	
CYP11B1EX7	52	C	0.99	T	0.01	0.03	CTGTGGGTCTGTTTYTGGAGCGAGTGGCG	CTG	TTG	Synonymous	Leu	Leu	
CYP11B1EX8	144	T	0.96	C	0.04	0.08	CCGGCAGGAACTTCYACCACGTGCCCTTT	TAC	CAC	Nonsynonymous	Tyr	His	
CYP11B1EX9	16	G	0.96	C	0.04	0.07	CCAGATGGAAACCCSGCTTCTGTCCTAGG	.	.	Other	Intron	.	
CYP11B1EX9	274	T	0.91	C	0.09	0.16	AGCCCCAGCACAAAYGGAACTCCCGAGGG	.	.	Other	3'UTR	.	
CYP11B1EX9	350	T	0.88	G	0.12	0.21	GCTGGGGAAGATCTKGCTGACCTTGTCCC	.	.	Other	3'UTR		
CYP11B1EX9	459	G	0.72	A	0.28	0.40	CCTCGTGTGGCCATRCAAGGGTGCTGTGG	.	.	Other	3'UTR	.	
CYP11B1EX9	592	A	0.93	C	0.07	0.13	TCTAGAGTCCAGTCMAGTTCCCTCCTGCA	.	.	Other	3'UTR	.	
CYP11B1EX9	62	C	0.99	T	0.01	0.03	GTGGAGACACTAACYCAAGAGGACATAAA	ACC	ACT	Synonymous	Thr	Thr	
CYP11B1EX9	657	G	0.66	A	0.34	0.45	CTCTGAAAGTTGTCRCCCCTGGAATAGGGT	.	.	Other	3'UTR	.	
CYP11B1EX9	786	A	0.87	G	0.13	0.22	ATCGTGTCAGCCTCRTGCCCCTGGCCTCA	.	.	Other	3'UTR	.	

CYP11B1EX9	835	C	0.77	T	0.23	0.35	GTTCCAGGAGTGGGYGTTGGGTCCTCTGC	.	.	Other	3'UTR	.	.	
CYP11B1EX9	879	A	0.68	G	0.32	0.44	CTGGGGAAGGTCCCRAGGATGCTGTCAGG	.	.	Other	3'UTR	.	.	
CYP11B2EX1	163	A	0.97	G	0.03	0.06	TCCTGGGTGAGATARAAGGATTTGGGCTG	.	.	Other	Promoter	.	.	
CYP11B2EX3	138	C	0.66	T	0.34	0.45	GTGGCCAGGGACTTYTCCCAGGCCCTGAA	TTC	TTT	Synonymous	Phe	Phe	Phe	
CYP11B2EX3	152	A	0.71	G	0.29	0.41	CTCCCAGGCCCTGARGAAGAAGGTGCTGC	AAG	AGG	Nonsynonymous	Lys	Arg	Arg	
CYP11B2EX3	20	G	0.98	C	0.03	0.05	CAAGCTCTGCCCTGSCCTCTGTAGGAATG	.	.	Other	Intron	.	.	
CYP11B2EX3	243	G	0.97	A	0.03	0.06	GGTGTGGGCCATGCRGGAAGGTCCAGCCC	.	.	Other	Intron	.	.	
CYP11B2EX4	177	T	0.96	C	0.04	0.07	CCTGTCTCGCTGGAYCAGCCCCAAGGTGT	ATC	ACC	Nonsynonymous	Ile	Thr	Thr	
CYP11B2EX4	250	G	0.98	A	0.02	0.04	GAGGCCAGGGACCCRGGCAGTGCTATGGG	.	.	Other	Intron	.	.	
CYP11B2EX4	99	A	0.94	C	0.06	0.12	TTCTGCCAGCCTGAMCTTCCTCCATGCCC	AAC	ACC	Nonsynonymous	Asn	Thr	Thr	
CYP11B2EX5	103	G	0.05	A	0.95	0.10	ACAGGCATCGTGGCRGAGCTCCTGTTGAA	GCG	GCA	Synonymous	Ala	Ala	Ala	
CYP11B2EX5	121	G	0.78	A	0.23	0.35	CTCCTGTTGAAGGCRGAACTGTCACTAGA	GCG	GCA	Synonymous	Ala	Ala	Ala	
CYP11B2EX5	55	C	0.99	T	0.01	0.02	ATCCAGAAAATCTAYCAGGAACTGGCCTT	TAC	TAT	Synonymous	Tyr	Tyr	Tyr	
CYP11B2EX5	72	A	0.99	G	0.01	0.02	GGAACTGGCCTTCARCCGCCCTCAACACT	AAC	AGC	Nonsynonymous	Asn	Ser	Ser	
CYP11B2EX6	195	A	0.84	C	0.16	0.27	TCAAGGAGACCTTGMGGTGGGTGCTGGCT	AGG	CGG	Synonymous	Arg	Arg	Arg	
CYP11B2EX6	91	T	0.38	C	0.63	0.47	CGACGTGCAGCAGAYCCTGCGCCCAGGAGA	ATC	ACC	Nonsynonymous	Ile	Thr	Thr	
CYP11B2EX7	52	T	0.99	C	0.01	0.03	CTGTGGGTCTGTTTYTGGAGCGAGTGGTG	TTG	CTG	Synonymous	Leu	Leu	Leu	
CYP11B2EX7	56	A	0.97	T	0.03	0.06	GGGTCTGTTTTTGGWGCGAGTGGTGAGCT	GAG	GTG	Nonsynonymous	Glu	Val	Val	
CYP11B2EX7	65	T	0.91	C	0.09	0.17	TTTGGAGCGAGTGGYGAGCTCAGACTTGG	GTG	GCG	Nonsynonymous	Val	Ala	Ala	
CYP11B2EX7	78	G	0.82	A	0.18	0.30	GTGAGCTCAGACTTRGTGCTTCAGAACTA	TTG	TTA	Synonymous	Leu	Leu	Leu	
CYP11B2EX8	132	G	0.97	A	0.03	0.06	ACATCAGGGGCTCCRGCAGGAACTTCCAC	GGC	AGC	Nonsynonymous	Gly	Ser	Ser	
CYP11B2EX8	18	C	0.99	T	0.01	0.02	TGATCCCTGCTCTGYACCGTCCGCAGACA	.	.	Other	Intron	.	.	
CYP11B2EX8	182	C	0.98	T	0.02	0.04	ATGCGCCAGTGCCTYGGGCGGCGCCTGGC	CTC	CTT	Synonymous	Leu	Leu	Leu	
CYP11B2EX8	37	T	0.99	A	0.01	0.02	TCCGCAGACATTGGWACAGGTTTTCCTCT	GTA	GAA	Nonsynonymous	Val	Glu	Glu	
CYP11B2EX9	224	G	0.89	A	0.11	0.20	GTCTTCTCTCCCACRTGCACAGCTTCCTG	.	.	Other	3'UTR	.	.	
CYP11B2EX9	90	T	0.99	G	0.01	0.03	AGATGGTCTACAGCKTCATATTGAGGCCT	TTC	GTC	Nonsynonymous	Phe	Val	Val	
DBHEX1	152	G	0.99	A	0.01	0.02	GGGCCAGCCTGCCCRGCCCCAGCATGCGG	.	.	Other	5'UTR	.	.	
DBHEX3	153	G	0.92	A	0.08	0.14	AGTTGCCCTCAGACRCGTGCACCATGGAG	GCG	ACG	Nonsynonymous	Ala	Thr	Thr	
DBHEX3	239	G	0.97	C	0.03	0.06	AAGGAGCTTCCAAASGGCTTCTCTCGGCA	AAG	AAC	Nonsynonymous	Lys	Asn	Asn	
DBHEX3	257	C	0.98	T	0.03	0.05	TTCTCTCGGCACCAYATTATCAAGGTACG	CAC	CAT	Synonymous	His	His	His	
DBHEX3	63	G	0.96	C	0.04	0.08	CGTTCCGGTCACTGSAGGCCATCAACGGC	GAG	CAG	Nonsynonymous	Glu	Gln	Gln	

DBIIEX4	12	G	0.96	C	0.04	0.08	CCTCCTCACAGTACSAGCCCAYCGTCACC	GAG	CAG	Nonsynonymous	Glu	Gln
DBIIEX4	132	G	0.94	A	0.06	0.11	CCAAGATGAAACCCRACCGCCTCAACTAC	GAC	AAC	Nonsynonymous	Asp	Asn
DBIIEX5	37	T	0.94	C	0.06	0.11	AGAGGAAGCCGGCCYTGCCTTCGGGGGTC	CTT	CCT	Nonsynonymous	Leu	Pro
DBIIEX5	39	G	0.94	T	0.06	0.11	AGGAAGCCGGCCTTKCCTTCGGGGGTCCA	GCC	TCC	Nonsynonymous	Ala	Ser
DDIR	122	A	0.84	G	0.16	0.27	CCTATTCCCTGCTTRGGAACTTGAGGGGT	.	.	Other	Promoter	.
DDIR	1521	G	0.96	A	0.04	0.08	CTGAACTCGCAGATRAATCCTGCCACACA	.	.	Other	3'UTR	.
DDIR	278	A	0.96	C	0.04	0.08	TGCTCATCCTGTCCMCGCTCCTGGGGAAC	ACG	CCG	Nonsynonymous	Thr	Pro
DDIR	279	C	0.99	G	0.01	0.02	GCTCATCCTGTCCASGCTCCTGGGGAACA	ACG	AGG	Nonsynonymous	Thr	Arg
DDIR	310	C	0.98	G	0.02	0.04	CTGGTCTGTGCTGCSGTTATCAGGTTCCG	GCC	GCG	Synonymous	Ala	Ala
DDIR	319	G	0.99	T	0.01	0.02	GCTGCCGTTATCAGKTTCCGACACCTGCG	AGG	AGT	Nonsynonymous	Arg	Ser
DDIR	76	G	0.98	A	0.03	0.05	GCAAAGTGCTGCCTRGTGGGGAGGACTCC	.	.	Other	Promoter	
DDIR	764	T	0.98	G	0.03	0.05	ATGCCATCTCATCCKCTGTAATAAGCTTT	TCT	GCT	Nonsynonymous	Ser	Ala
EDNRAEX6	124	A	0.28	G	0.72	0.40	ACTGTGTATAACGARATGGACAAGAACCG	GAA	GAG	Synonymous	Glu	Glu
EDNRAEX6	88	C	0.31	T	0.69	0.43	TGGTTCCCTCTTCAYTTAAGCCGTATATT	CAC	CAT	Synonymous	His	His
EDNRAEX8	1157	G	0.66	A	0.34	0.45	TTTTCAGATGATTCRGAAATTTTCATTCA	.	.	Other	3'UTR	.
EDNRAEX8	1380	C	0.52	T	0.48	0.50	ACGATTCTTCACTTYTTGGGGTTTTCAGT	.	.	Other	3'UTR	
EDNRAEX8	1687	A	0.83	G	0.17	0.28	TTGTGCCAAAGTGCRTAGTCTGAGCTAAA	.	.	Other	3'UTR	.
EDNRAEX8	228	C	0.47	G	0.53	0.50	CAAGGCAACTGTGASTCCGGGAATCTCTT	.	.	Other	3'UTR	.
EDNRAEX8	295	A	0.99	G	0.01	0.02	AAGAAATGCTTTCCRAAACCGCAAGGTAG	.	.	Other	3'UTR	.
EDNRAEX8	622	G	0.38	A	0.62	0.47	ACAATATGGGCTCARGTCACTTTTATTTG	.	.	Other	3'UTR	.
EDNRAEX8	655	G	0.99	A	0.01	0.03	GTCATTTGGTGCCARTATTTTTTAACTGC	.	.	Other	3'UTR	.
EDNRAEX8	788	A	0.88	G	0.12	0.21	CTATTTATTTTTTTRAAACACAAATTCTA	.	.	Other	3'UTR	.
EDNRAEX8	950	T	0.96	C	0.04	0.08	GAACATGTTTTGTAYGTTAAATTCAAAAG	.	.	Other	3'UTR	.
EDNRAEX8	985	T	0.97	C	0.03	0.06	TTCAATCAGATAGTYCTTTTTTCACAAGTT	.	.	Other	3'UTR	.
EDNRBEX1	33	T	0.98	A	0.03	0.05	GCCGCCTCCAAGTCWGTGCGGACGCGCCC	CTG	CAG	Nonsynonymous	Leu	Gln
EDNRBEX1	347	T	0.99	G	0.01	0.02	TGTCCTGCCTTGTGKTCGTGCTGGGGATC	TTC	GTC	Nonsynonymous	Phe	Val
EDNRBEX1	62	C	0.99	T	0.01	0.02	TGGTTGCGCTGGTTYTTGCCTGCGGCCTG	CTT	TTT	Nonsynonymous	Leu	Phe
EDNRBEX2	78	C	0.95	T	0.05	0.10	ATACAGAAAGCCTCYGTGGGAATCACTGT	TCC	TCT	Synonymous	Ser	Ser
EDNRBEX2	87	C	0.99	T	0.01	0.03	GCCTCCGTGGGAATYACTGTGCTGAGTCT	ATC	ATT	Synonymous	Ile	Ile
EDNRBEX3	144	C	0.94	T	0.06	0.11	TTTTGATATAATTAYGATGGACTACAAAG	ACG	ATG	Nonsynonymous	Thr	Met
EDNRBEX4	122	G	0.99	A	0.01	0.03	GTTGAGAAAGAAAARTGGCATGCAGATTG	AGT	AAT	Nonsynonymous	Ser	Asn

EDNRBEX4	39	G	0.82	A	0.18	0.29	AAAGATTGGTGGCTRTTCAGTTTCTATTT	CTG	CTA	Synonymous	Leu	Leu
ELAM1EX1	143	A	0.93	G	0.07	0.13	TCTTTGACCTAAATRATGAAAGTCTTAAA	.	.	Other	Promoter	.
ELAM1EX1	209	T	0.97	G	0.03	0.06	TTATTGCACTAGTGKCCTTTGCCCAAAT	.	.	Other	Promoter	.
ELAM1EX10	107	C	0.91	T	0.09	0.16	CATTAGCACCATTTYTCCTCTGGCTTCGG	CTC	TTC	Nonsynonymous	Leu	Phe
ELAM1EX12	54	T	0.96	C	0.04	0.08	AGCCTTGAATCAGAYGGAAGCTACCAAAA	GAT	GAC	Synonymous	Asp	Asp
ELAM1EX13	1004	T	0.98	G	0.02	0.04	CAGAAATATGTGGTKTCCACGATGAAAAA	.	.	Other	3' UTR	.
ELAM1EX13	1158	G	0.18	A	0.82	0.29	GATGTTTGTCAGATRTGATATGTAAACAT	.	.	Other	3' UTR	.
ELAM1EX13	1549	G	0.39	A	0.61	0.47	TGAACACTGGCAACRACAAAGCCAACAGT	.	.	Other	3' UTR	.
ELAM1EX13	967	T	0.97	C	0.03	0.06	ACTGAATGGAAGGTYTGTATATTGTCAGA	.	.	Other	3' UTR	.
ELAM1EX2	382	C	0.98	G	0.02	0.04	AATGATGAGAGGTGSAGCAAGAAGAAGCT	TGC	TGG	Nonsynonymous	Cys	Trp
ELAM1EX3	152	T	0.95	C	0.05	0.10	GTAAGTCTGGTTCTYGCCTCTTTCTTCAC	.	.	Other	Intron	.
ELAM1EX3	53	A	0.97	C	0.03	0.06	CCAATACATCCTGCMGTGGCCACGGTGAA	AGT	CGT	Nonsynonymous	Ser	Arg
ELAM1EX5	197	G	0.95	A	0.05	0.10	GGAATTGGGACAACRAGAAGCCAACGTGT	GAG	AAG	Nonsynonymous	Glu	Lys
ELAM1EX5	55	T	0.97	C	0.03	0.06	GATGCTGTGACAAAYCCAGCCAATGGGTT	AAT	AAC	Synonymous	Asn	Asn
ELAM1EX7	199	C	0.94	T	0.06	0.12	GGGGAGTGGGACAAYGAGAAGCCCACATG	AAC	AAT	Synonymous	Asn	Asn
ELAM1EX7	200	G	0.94	C	0.06	0.11	GGGAGTGGGACAACSAGAAGCCCACATGT	GAG	CAG	Nonsynonymous	Glu	Gln
ELAM1EX8	152	C	0.96	T	0.04	0.08	AGGGATTTGAATTAYATGGATCAACTCAA	CAT	TAT	Nonsynonymous	His	Tyr
ELAM1EX8	22	T	0.91	C	0.09	0.16	AGTGCTCTCTCGTGYGTTCCAGCTGTGAG	.	.	Other	Intron	.
ENDOTHELIN2	440	T	0.97	C	0.03	0.07	CCCCTGCAGACGTGYTCCAGACTGGCAAG	TTC	CTC	Nonsynonymous	Phe	Leu
ENDOTHELIN2	556	G	0.99	A	0.01	0.02	ATGCGGGAGCCTCGRTCCACACATTCCAG	CGG	CGA	Synonymous	Arg	Arg
ENDOTHELIN2	976	A	0.84	G	0.16	0.27	AGCCAGCCCTGGAGRCTGGATGGCTCCCC	.	.	Other	3' UTR	.
ETIEX3	114	G	0.88	A	0.12	0.21	GCAACAGACCGTGARAATAGATGCCAATG	GAG	GAA	Synonymous	Glu	Glu
ETIEX5	90	G	0.69	T	0.31	0.43	AAGCTGAAAGGCAAKCCCTCCAGAGAGCG	AAG	AAT	Nonsynonymous	Lys	Asn
GALNREX1	1052	G	0.94	T	0.06	0.11	CTGCCCACCTGGGTKCTGGGCGCCTTCAT	GTG	GTT	Synonymous	Val	Val
GALNREX1	325	C	0.98	G	0.02	0.04	GGTGCAGCACGCAGSCGCTCCGGGAGCCA	.	.	Other	Promoter	.
GALNREX1	327	G	0.81	C	0.19	0.30	TGCAGCACGCAGCCSCTCCGGGAGCCAGG	.	.	Other	Promoter	.
GALNREX1	553	G	0.49	C	0.51	0.50	TCTCTCAGAAGGTCSCGGCGCCAAAGACGG	.	.	Other	Promoter	.
GALNREX1	887	C	0.49	T	0.51	0.50	ATCTTCGCGCTGGGYGTGCTGGGCAACAG	GGC	GGT	Synonymous	Gly	Gly
GALNREX3	298	A	0.68	G	0.32	0.43	TGATACTAAAGAAARTAAAAGTCGAATAG	AAT	AGT	Nonsynonymous	Asn	Ser
GALNREX3	322	C	0.98	T	0.02	0.04	AATAGACACCCCACYATCAACCAATTGTA	CCA	CTA	Nonsynonymous	Pro	Leu
GALNREX3	388	T	0.98	C	0.02	0.04	AGTTTCCATATAAGYGGACCAGACACAGA	.	.	Other	3' UTR	.

GALNREX3	418	C	0.97	G	0.03	0.06	ACAAACAGAATGAGSTAGTAAGCGATGCT	.	.	Other	3'UTR	.	
GALNREX3	523	G	0.98	T	0.02	0.04	TAGGAAATTCCTAGKTCTAGTGAGAATTA	.	.	Other	3'UTR	.	
GALNREX3	650	C	0.94	T	0.06	0.11	TCCATATATATGTTYAACTCTTCATAGAT	.	.	Other	3'UTR	.	
GALNREX3	799	A	0.84	G	0.16	0.26	ATGTATTTTAAAATRTGATCATGGACACA	.	.	Other	3'UTR	.	
GGREX1	125	G	0.98	A	0.02	0.04	CTGCTGTTGCTGCTRCTGCTGGCCTGCCA	CTG	CTA	Synonymous	Leu	Leu	
GGREX11	57	C	0.91	T	0.09	0.16	CACGAAGTGGTCTTYGCCTTCGTGACGGA	TTC	TTT	Synonymous	Phe	Phe	
GGREX4	68	C	0.98	G	0.02	0.05	GACCCCGGGGGCAGSCTTGGCGTGATGCC	CCT	GCT	Nonsynonymous	Pro	Ala	
GGREX5	71	C	0.83	G	0.17	0.28	CTGTCCCTGGGGGCSCTGCTCCTCGCCTT	GCC	GCG	Synonymous	Ala	Ala	
GGREX9	29	T	0.93	G	0.07	0.12	TGACAACATGGGCTKCTGGTGGATCCTGC	TTC	TGC	Nonsynonymous	Phe	Cys	
GH1EX4	144	G	0.98	A	0.02	0.03	CCTCTGACAGCAACRTCTATGACCTCCTA	GTC	ATC	Nonsynonymous	Val	Ile	
GH2EX3	126	A	0.94	T	0.06	0.12	CAACACCTTCCAACWGGGTGAAAACGCAG	AGG	TGG	Nonsynonymous	Arg	Trp	
GIPREX2	72	C	0.93	G	0.08	0.14	CTTCGCCGCCCCTCASGATGACTACCTCTC	.	.	Other	5'UTR	.	
GIPREX7	51	C	0.79	T	0.21	0.33	CATTGCACTAGAAAYTATATCCACATCAA	AAC	AAT	Synonymous	Asn	Asn	
GIPREX8	180	C	0.98	G	0.03	0.05	GCTACTACCTGCTCSTCGGCTGGGGTGAG	CTC	GTC	Nonsynonymous	Leu	Val	
GLUT2EX1	137	C	0.32	A	0.68	0.44	CCACAGCACTAATTMTCTGTGGAGCAGAG	.	.	Other	Promoter	.	
GLUT2EX1	164	T	0.31	C	0.69	0.43	AGTGCAGTGTGCCTYCCATGCTCCACAGC	.	.	Other	Promoter	.	
GLUT2EX1	237	T	0.96	C	0.04	0.07	AAAGATTTCTCTTTYCACCGGCTCCCAAT	.	.	Other	Promoter	.	
GLUT2EX1	242	G	0.34	A	0.66	0.45	TTTCTCTTTTCACCRGCTCCCAATTACTG	.	.	Other	Promoter	.	
GLUT2EX10	161	G	0.99	A	0.01	0.02	GAATTCCAAAAGAARAGTGGCTCAGCCCA	AAG	AAA	Synonymous	Lys	Lys	
GLUT2EX10	87	C	0.99	G	0.01	0.03	TCCTGGCCTTTACCSTGTTTACATTTTTT	CTG	GTG	Nonsynonymous	Leu	Val	
GLUT2EX10	92	T	0.35	C	0.65	0.46	GCCTTTACCCTGTTYACATTTTTTAAAGT	TTT	TTC	Synonymous	Phe	Phe	
GLUT2EX3	250	C	0.87	T	0.13	0.23	AGTTGGTGGAATGAYTGCATCATTCTTTG	ACT	ATT	Nonsynonymous	Thr	Ile	
GLUT2EX4A	153	T	0.96	C	0.04	0.08	TCAGGACTATATTGYGGTAAGTCTCACAC	TGT	TGC	Synonymous	Cys	Cys	
GLUT2EX4A	162	T	0.83	A	0.17	0.28	TATTGTGGTAAGTCWCACACACACACACA	.	.	Other	Intron	.	
GLUT2EX4A	164	A	0.94	T	0.06	0.11	TTGTGGTAAGTCTCWCACACACACACACA	.	.	Other	Intron	.	
GLUT2EX4B	127	A	0.28	G	0.72	0.40	CTGGCCATCGTCACRGGCATTCTTATTAG	ACA	ACG	Synonymous	Thr	Thr	
GLUT2EX5	78	C	0.93	T	0.08	0.14	ATCTGTGGCACATCYTGCTTGGCCTGTCT	CTG	TTG	Synonymous	Leu	Leu	
GLUT2EX6	15	T	0.10	C	0.90	0.18	TGTTTCAACCTGATYATTTTCTTGGACAG	.	.	Other	Intron	.	
GLUT2EX8	21	T	0.88	C	0.12	0.21	TAATTTCTTTAAAAYTGTCCTAGGTATTC	.	.	Other	Intron	.	
GLUT2EX8	38	T	0.95	C	0.05	0.10	TCCTAGGTATTCCTYGTGGAGAAGGCAGG	CTT	CTC	Synonymous	Leu	Leu	
GLUT4EX1	1002	A	0.99	C	0.01	0.02	CGTTGTGGGAACGGMATTTCCTGGCCCCC	.	.	Other	Promoter	.	

GLUT4EX1	1051	C	0.74	T	0.26	0.38	AGCATGTCGCGGACYCTTTAAGGCGTCAT	.	.	.	Other	Promoter	.	.	.
GLUT4EX1	1228	A	0.86	T	0.14	0.24	TCTCAGGCCCGCTGGWGTTTCCCCGGGGCA	.	.	.	Other	Promoter	.	.	.
GLUT4EX1	1632	A	0.71	C	0.29	0.42	CAGCCCCGCTCCACMAGATCCGCGGGAGC	.	.	.	Other	5' UTR	.	.	.
GLUT4EX1	1662	A	0.64	G	0.36	0.46	CCACTGCTCTCCGGRTCCTTGGCTTGTGG	.	.	.	Other	5' UTR	.	.	.
GLUT4EX1	1683	G	0.98	C	0.02	0.05	GCTTGTGGCTGTGGSTCCCATCGGGCCCG	.	.	.	Other	5' UTR	.	.	.
GLUT4EX1	1691	G	0.94	A	0.06	0.11	CTGTGGGTCCCATCRGGCCCGCCCTCGCA	.	.	.	Other	Promoter	.	.	.
GLUT4EX1	368	G	0.96	A	0.04	0.07	ACAGGAGGAATCGARCCTGACTTCTACCA	.	.	.	Other	Promoter	.	.	.
GLUT4EX1	560	A	0.90	G	0.10	0.19	GCGGAAAGGCGAGARATAGTGGGTTGAGA	.	.	.	Other	Promoter	.	.	.
GLUT4EX1	615	G	0.93	A	0.07	0.14	TCGCTCGCCCTCCARGTGGCAGCACAACC	.	.	.	Other	Promoter	.	.	.
GLUT4EX1	91	C	0.95	T	0.05	0.10	CAGGAGGTTTTGTTYACTCTGAAAAGGGA	.	.	.	Other	Promoter	.	.	.
GLUT4EX1	966	C	0.95	A	0.05	0.10	CTGAAAGACAGGACMAAGCAGCCCGGCCA	.	.	.	Other	Promoter	.	.	.
GLUT4EX10	19	C	0.94	G	0.06	0.11	TCCACCCTCCCTGTSTGGCCCCTAGGAGC	.	.	.	Other	Intron	.	.	.
GLUT4EX11	1005	G	0.83	A	0.17	0.28	GTGCTGGGATTACARGCGTGAGCCACCGC	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	1099	A	0.95	C	0.05	0.10	GAAAGTATGTGCCCMTGTGTGGCAAGATG	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	791	T	0.93	C	0.07	0.14	CGAGTGCAGTGGCGYGATCTTGCTTCACT	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	827	C	0.90	T	0.10	0.18	GTCTCCCAGGTTCAYGCCATTCTCCTGCC	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	872	G	0.79	A	0.21	0.33	CTGGGACTACAGGCRCATGCCACCACACC	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	874	A	0.92	C	0.08	0.15	GGGACTACAGGCGCMTGCCACCACACCTG	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	884	A	0.73	G	0.27	0.40	GCGCATGCCACCACRCCTGGCTAATTTAT	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	897	A	0.89	T	0.11	0.20	CACCTGGCTAATTTWTTTTGTATTTTTAG	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	930	A	0.88	G	0.13	0.22	TACGCGGTTTCACCRTGTTAGCCAGAATG	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	935	A	0.86	G	0.14	0.24	GGTTTCACCATGTTRGCCAGAATGGTCTC	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	941	A	0.49	G	0.51	0.50	ACCATGTTAGCCAGRATGGTCTCGAYCTC	.	.	.	Other	3' UTR	.	.	.
GLUT4EX11	963	C	0.96	T	0.04	0.07	CGATCTCCTGACCTYGTGATCTGCCTGCC	.	.	.	Other	3' UTR	.	.	.
GLUT4EX3	112	C	0.90	G	0.10	0.17	TCCAGGCACCCTCASCACCCTCTGGCCCC	ACC	AGC	Nonsynonymous	Thr	Ser			
GLUT4EX4	96	C	0.71	T	0.29	0.42	ATGGGCCTGGCCAAYGCTGCTGCCTCCTA	AAC	AAT	Synonymous	Asn	Asn			
GLUT4EX7	19	C	0.95	T	0.05	0.09	TCAGGCCTGACCTTYCCTCTCCAGGTCT	.	.	.	Other	Intron	.	.	.
GLUT4EX7	227	G	0.99	C	0.01	0.02	ATGCTGTATGTGTGSAGCAGCCTCCAGGC	.	.	.	Other	Intron	.	.	.
GLUT5EX1	184	G	0.95	A	0.05	0.10	AAAAGGAGGTGAGCRGCACTCTGCCCTTC	.	.	.	Other	5' UTR	.	.	.
GNB3EX1	184	A	0.89	C	0.11	0.20	GACAGATGGGGAACMCTGTGCCTCCCTGA	.	.	.	Other	Promoter	.	.	.
GNB3EX1	201	A	0.63	G	0.37	0.47	GTGCCTCCCTGAACRGAAATGGCAGGGGA	.	.	.	Other	Promoter	.	.	.

GNB3EX1	328	A	0.63	G	0.37	0.47	GCCAGGGGCCAGTCRAGTGTATCACAGAT	.	.	Other	Promoter	.		
GNB3EX10	144	G	0.93	A	0.07	0.13	AGAGCATCATCTGCRGCATCACGTCCGTG	GGC	AGC	Nonsynonymous	Gly	Ser		
GNB3EX10	155	C	0.61	T	0.39	0.48	TGCGGCATCACGTCYGTGGCCTTCTCCCT	TCC	TCT	Synonymous	Ser	Ser		
GNB3EX11	129	G	0.97	T	0.03	0.06	CTTCCTCAAAATCTKGAACTGAGGAGGCT	TGG	TTG	Nonsynonymous	Trp	Leu		
GNB3EX11	254	C	0.75	T	0.25	0.38	CCACTAAGCTTTCTYCTTTGAGGGCAGTG	.	.	Other	3' UTR	.		
GNB3EX11	536	C	0.60	T	0.40	0.48	TATGGCTCTGGCACYACTAGGGTCCTGGC	.	.	Other	3' UTR	.		
GSY1EX10	46	A	0.99	G	0.01	0.02	GGAGCCTTCCCGACRTGAACAAGATGCTG	ATG	GTG	Nonsynonymous	Met	Val		
GSY1EX12	152	A	0.95	G	0.05	0.10	CCTTGGGGCTACACRCCGGGTGAGTGTAG	ACA	ACG	Synonymous	Thr	Thr		
GSY1EX12	163	G	0.95	A	0.05	0.09	CACACCGGGTGAGTRTAGTGGGCAGGGGA	.	.	Other	Intron	.		
GSY1EX15	75	G	0.96	C	0.04	0.07	CCAAGGCCTTTCCASAGCACTTCACCTAC	GAG	CAG	Nonsynonymous	Glu	Gln		
GSY1EX16	152	C	0.99	T	0.01	0.02	CCGCTGGAGGAAGAYGGCGAGCGCTACGA	GAC	GAT	Synonymous	Asp	Asp		
GSY1EX16	210	C	0.94	G	0.06	0.11	GCAACATCCGTGCASCAGAGTGGCCGCGC	CCA	GCA	Nonsynonymous	Pro	Ala		
GSY1EX16	65	G	0.94	A	0.06	0.11	CGGCCAGCCTCGGTRCCACCGTCGCCCTC	GTG	GTA	Synonymous	Val	Val		
GSY1EX2	219	G	0.99	A	0.01	0.03	CTGCAAGGTGGGACRTGGCCCAGCCCAGG	.	.	Other	Intron	.		
GSY1EX3	117	A	0.95	G	0.05	0.10	CCCTGGAGCGCTGGRAGGGAGAGCTCTGG	AAG	GAG	Nonsynonymous	Lys	Glu		
GSY1EX3	134	T	0.96	C	0.04	0.08	GGAGAGCTCTGGGAYACCTGCAACATCGG	GAT	GAC	Synonymous	Asp	Asp		
GSY1EX3	149	A	0.95	G	0.05	0.10	ACCTGCAACATCGGRGTGCCGTGGTACGA	GGA	GGG	Synonymous	Gly	Gly		
GSY1EX3	53	C	0.99	G	0.01	0.03	GGGCGCTGGCTGATSGAGGGAGGCCCTCT	ATC	ATG	Nonsynonymous	Ile	Met		
GSY1EX4	16	C	0.93	T	0.07	0.12	ACAGTGGCCCTGTCYCTGTTGCCCACAGT	.	.	Other	Intron	.		
GSY1EX5	44	G	0.96	A	0.04	0.08	TTCAACGTGGACAARGAAGCAGGGGAGAG	AAG	AAA	Synonymous	Lys	Lys		
GSY1EX6	54	A	0.99	G	0.01	0.03	CCCCAATGGGCTGARTGTGAAGAAGTTTT	AAT	AGT	Nonsynonymous	Asn	Ser		
GSY1EX7	114	C	0.71	T	0.29	0.42	GGTGCTGACGTCTTYCTGGAGGCATTGGC	TTC	TTT	Synonymous	Phe	Phe		
GSY1EX7	16	T	0.98	G	0.02	0.04	GCTTTACCGTGCCTKGTGGGTTCTTTAGG	.	.	Other	Intron	.		
GSY1EX7	17	G	0.99	C	0.01	0.02	CTTTACCGTGCCTTSTGGGTTCTTTAGGC	.	.	Other	Intron	.		
GSY1EX8	43	A	0.94	G	0.06	0.11	GGTGAACGGCAGCGRGCAGACAGTGGTTG	GAG	GGG	Nonsynonymous	Glu	Gly		
HAPTEX1	135	T	0.97	C	0.03	0.06	GATAAAGAGACAGAYTGATGGTTCCTGCC	.	.	Other	5' UTR	.		
HAPTEX1	188	C	0.90	T	0.10	0.18	GATTTCAGGAAATAYTTTGGCAGGTTTGT	.	.	Other	5' UTR	.		
HAPTEX1	239	T	0.95	G	0.05	0.09	CTTGGGATTTGTAAKAGAACATCACAAGA	.	.	Other	5' UTR	.		
HAPTEX1	326	T	0.45	A	0.55	0.50	ACTGGAAAAGATAGWGACCTTACCAGGGC	.	.	Other	5' UTR	.		
HAPTEX1	329	C	0.76	G	0.24	0.37	GGAAAAGATAGTGASCTTACCAGGGCCAA	.	.	Other	5' UTR	.		
HAPTEX1	369	A	0.88	C	0.12	0.21	ACAGGAATTACGAAMTGGAGAAGGGGGAG	.	.	Other	5' UTR	.		

HAPTEX1	375	A	0.89	G	0.11	0.19	ATTACGAAATGGAGRAGGGGGGAGAAGTGA	.	.	Other	5' UTR	.	
HAPTEX4	34	A	0.53	G	0.47	0.50	TTTGTTTCAGGAGTRTACACCTTAAATGA	GTA	GTG	Synonymous	Val	Val	
HAPTEX6	34	G	0.66	A	0.34	0.45	TTTGTTTCAGGAGTRTACACCTTAAACAA	GTA	GTG	Synonymous	Val	Val	
HAPTEX7	1331	C	0.98	T	0.02	0.03	CATGCTGTTGCCTCYTCAAAGTGAATTAG	.	.	Other	3' UTR	.	
HAPTEX7	367	G	0.98	A	0.02	0.03	GTGTCTGTTAATGARAGAGTGATGCCCAT	GAG	GAA	Synonymous	Glu	Glu	
HAPTEX7	610	T	0.98	C	0.02	0.04	CACACCTTCTGTGCYGGCATGTCTAAGTA	GCT	GCC	Synonymous	Ala	Ala	
HAPTEX7	673	C	0.98	T	0.02	0.03	GCCTTTGCCGTTCAYGACCTGGAGGAGGA	CAC	CAT	Synonymous	His	His	
HSD11KEX2	232	C	0.95	A	0.05	0.10	ACCAAGGCCCACACMACCAGCACCGGTCA	ACC	ACA	Synonymous	Thr	Thr	
HSD11KEX3	139	G	0.83	A	0.18	0.29	AATTTCTTTGGCGCRCTCGAGCTGACCAA	GCG	GCA	Synonymous	Ala	Ala	
HSD11KEX5	951	T	0.96	A	0.04	0.08	ACTGTACTTCCCAAWTGCCACATTTTAAA	.	.	Other	3' UTR	.	
HSTSCGENE	1392	C	0.97	T	0.03	0.06	ATCTTCGGGGCCACYCTCTCCTCTGCCCT	ACC	ACT	Synonymous	Thr	Thr	
HSTSCGENE	1881	G	0.98	A	0.02	0.03	GCCCTCAGCTACTCRGTGGGCCTCAATGA	TCG	TCA	Synonymous	Ser	Ser	
HSTSCGENE	2139	C	0.88	T	0.13	0.22	TCGGATGTCATTGCYGAGGACCTCCGCAG	GCC	GCT	Synonymous	Ala	Ala	
HSTSCGENE	2595	C	0.90	T	0.10	0.18	CGTGTGTTCGTAGGYGGCCAGATTAACAG	GGC	GGT	Synonymous	Gly	Gly	
HSTSCGENE	3269	G	0.81	A	0.19	0.30	GGTCTTGTGTTTATRGGCTAGAGAAATAG	.	.	Other	3' UTR	.	
HSTSCGENE	3660	C	0.94	T	0.06	0.11	CTGCAACCTCCTCCYGGGTTCAAGCATTT	.	.	Other	3' UTR	.	
HSTSCGENE	3710	G	0.98	C	0.02	0.03	TAGCTGGGATTACASGCACCTGCCATCAC	.	.	Other	3' UTR	.	
HSTSCGENE	3727	C	0.69	G	0.31	0.43	ACCTGCCATCACACSAGCTAATTTTTGTA	.	.	Other	3' UTR	.	
HSTSCGENE	3838	G	0.90	A	0.10	0.18	CCCAAAGTGCTGGGRTTACAGGCGTGAGC	.	.	Other	3' UTR	.	
HUMAPNIIA	3057	T	0.92	C	0.08	0.15	AGGGCATCTCTGAGYGTCTCTGCCTGGAG	.	.	Other	3' UTR	.	
HUMGFAT	2930	T	0.65	G	0.35	0.45	ATCTCCTAAAAGTGKTTTTTATTTCCTTG	.	.	Other	3' UTR	.	
HUMGLUTRN	2110	G	0.94	C	0.06	0.12	GGCTATGGCCACCCSTTCTGCTGGCCTGG	.	.	Other	3' UTR	.	
HUMGLUTRN	933	A	0.99	C	0.01	0.02	GATGATGCGGGAGAMGAAGGTCACCATCC	AAG	ACG	Nonsynonymous	Lys	Thr	
HUMGUANCYC	2388	C	0.93	T	0.07	0.14	ATTGTCACTGAATAYTGTCCTCGTGGGAG	TAC	TAT	Synonymous	Tyr	Tyr	
HUMGUANCYC	2571	A	0.86	G	0.14	0.24	CGTTTTGTGCTCAARATCACAGACTATGG	AAA	AGA	Nonsynonymous	Lys	Arg	
HUMGUANCYC	2643	G	0.93	A	0.07	0.14	GCCCTCTATGCCAARAAGCTGTGGACTGC	AAG	AAA	Synonymous	Lys	Lys	
HUMGUANCYC	2787	C	0.93	G	0.07	0.13	GAGGGCCTGGACCTSAGCCCCAAAGAGAT	CTC	CTG	Synonymous	Leu	Leu	
HUMGUANCYC	2905	C	0.97	G	0.03	0.07	AGCGATGTTGGGCTSAGGACCCAGCTGAG	CAG	GAG	Nonsynonymous	Gln	Glu	
HUMGUANCYC	3300	C	0.81	G	0.19	0.31	GACAACTTTGATGTSTACAAGGTGGAGAC	GTC	GTG	Synonymous	Val	Val	
HUMGUANCYC	3663	G	0.96	A	0.04	0.08	CTTCGGGGGGATGTRGAAATGAAGGGAAA	GTG	GTA	Synonymous	Val	Val	
IAPPEX1-2	199	T	0.97	C	0.03	0.06	TTTATTTAGAGAAAYGCACACTTGGTGTT	.	.	Other	Intron	.	

IAPPEX1-2	358	A	0.99	C	0.01	0.02	GACTGTATCAATAAMAATTTTGATCCTTG	.	.	Other	Intron	.	.	.
IAPPEX3	1050	T	0.83	C	0.18	0.29	TAAAGTCTATTGTTYGTTGTGCTTGCTGG	.	.	Other	3' UTR	.	.	.
IAPPEX3	1076	T	0.75	A	0.25	0.38	TGGTACTAAGAGGCWATTTAAAAGTATAA	.	.	Other	3' UTR	.	.	.
IAPPEX3	1184	A	0.66	C	0.34	0.45	TTTAAGTGGCTTTCMGCAAACCTCAGTCA	.	.	Other	3' UTR	.	.	.
IAPPEX3	296	C	0.85	T	0.15	0.26	TGCCCTTTTCATCTYCAGTGTGAATATAT	.	.	Other	3' UTR	.	.	.
IAPPEX3	848	G	0.11	A	0.89	0.19	CTCCAGCCTGGGTGRCAGAGTGAGACTCG	.	.	Other	3' UTR	.	.	.
IAPPEX3	959	A	0.93	G	0.07	0.13	TTCCTTTTTGCAGTRTATTTCTGAAATGA	.	.	Other	3' UTR	.	.	.
ICAM1EX1	683	A	0.66	C	0.34	0.45	AGAGTTGCAACCTCMGCCTCGCTATGGCT	.	.	Other	Promoter	.	.	.
ICAM1EX2	115	A	0.70	T	0.30	0.42	CTGTGACCAGCCCAWGTTGTTGGGCATAG	AAG	ATG	Nonsynonymous	Lys	Met	Met	Met
ICAM1EX3	151	G	0.99	C	0.01	0.02	CTCCGTGGGGAGAASGAGCTGAAACGGGA	AAG	AAC	Nonsynonymous	Lys	Asn	Asn	Asn
ICAM1EX4	115	G	0.92	T	0.08	0.15	TGTTCCCTGGACGGKCTGTTCCCAGTCTC	GGG	GGT	Synonymous	Gly	Gly	Gly	Gly
ICAM1EX4	238	C	0.95	T	0.05	0.10	GTGACCGCAGAGGAYGAGGGCACCCAGCG	GAC	GAT	Synonymous	Asp	Asp	Asp	Asp
ICAM1EX5	47	G	0.99	A	0.01	0.02	TTCCGGCGCCCCAACRTGATTCTGACGAAG	GTG	ATG	Nonsynonymous	Val	Met	Met	Met
ICAM1EX6	18	G	0.94	A	0.06	0.12	CATGTCATCTCATCRTGTTTTTCCAGATG	.	.	Other	Intron	.	.	.
ICAM1EX6	254	G	0.45	A	0.55	0.50	GGGAGGTCACCCGCRAGGTGACCGTGAAT	GAG	AAG	Nonsynonymous	Glu	Lys	Lys	Lys
ICAM1EX6	39	G	0.95	A	0.05	0.10	TCCAGATGGCCCCCRACTGGACGAGAGGG	CGA	CAA	Nonsynonymous	Arg	Gln	Gln	Gln
ICAM1EX7	304	C	0.99	T	0.01	0.03	GCAGCTACACCTACYGGCCCTGGGACGCC	.	.	Other	3' UTR	.	.	.
ICAM1EX7	869	A	0.99	G	0.01	0.03	TGGCAAAAAGATCARATGGGGCTGGGACT	.	.	Other	3' UTR	.	.	.
ICAM1EX7	929	T	0.96	C	0.04	0.07	GAGTGATTTTTCTAYCGGCACAAAAGCAC	.	.	Other	3' UTR	.	.	.
ICAM2EX1	300	C	0.99	T	0.01	0.02	GAGATGTCCTCTTTYGGTTACAGGACCCT	TTC	TTT	Synonymous	Phe	Phe	Phe	Phe
ICAM2EX2	63	G	0.93	A	0.07	0.13	GGCCAAAGAAGCTGRCGGTTGAGCCCAAA	GCG	ACG	Nonsynonymous	Ala	Thr	Thr	Thr
ICAM2EX3	281	G	0.98	A	0.03	0.05	GGACTTGATGTCTCRCGGTGGCAACATCT	CGC	CAC	Nonsynonymous	Arg	His	His	His
INSEX1	233	T	0.39	A	0.61	0.48	CAGCCCTGCCTGTCWCCCAGATCACTGTC	.	.	Other	5' UTR	.	.	.
INSEX1	247	C	0.97	T	0.03	0.06	TCCCAGATCACTGTYCTTCTGCCATGGCC	.	.	Other	5' UTR	.	.	.
INSEX1	453	C	0.78	T	0.22	0.34	CAGGGTGAGCCAACYGCCCATTGCTGCCC	.	.	Other	Intron	.	.	.
INSEX2	14	C	0.99	T	0.01	0.02	GAACCTGCTCTGCGYGGCACGTCCTGGCA	.	.	Other	Intron	.	.	.
KALSTEX1	133	G	0.88	T	0.12	0.21	CTGCTCCTCCTGCTKGTTGGACTACTGGC	CTG	CTT	Synonymous	Leu	Leu	Leu	Leu
KALSTEX1	511	A	0.89	G	0.11	0.19	CATGGGCTGGAAACRCGCGTGGGCAGTGC	ACA	ACG	Synonymous	Thr	Thr	Thr	Thr
KALSTEX2	318	A	0.67	T	0.33	0.44	GTAATCAGTGTGCTWTGGGGGCTGAATCT	.	.	Other	Intron	.	.	.
KALSTEX2	79	C	0.72	T	0.28	0.40	ACTCCCAAAGACTTYTATGTTGATGAGAA	TTC	TTT	Synonymous	Phe	Phe	Phe	Phe
KALSTEX3	17	A	0.98	G	0.02	0.05	AATGTTCTAACTCARTGCCCCTTTCAGGA	.	.	Other	Intron	.	.	.

KALSTEX3	91	T	0.97	C	0.03	0.07	CTGGCTCCTATGTAYTAGATCAGATTTTG	TTA	CTA	Synonymous	Leu	Leu
KLKEX1	105	G	0.98	T	0.02	0.03	AGGGCATTCTGAAGKCCAAGGCTTATATT	.	.	Other	5' UTR	.
KLKEX3	253	C	0.68	G	0.32	0.44	TGGAGTTGCCCACCSAGGAACCYGAAGTG	CAG	GAG	Nonsynonymous	Gln	Glu
KLKEX3	50	G	0.98	A	0.02	0.03	GCTCTGGCTGGGTCRCCCACAACTTGTTG	CGC	CAC	Nonsynonymous	Arg	His
KLKEX4	110	T	0.97	A	0.03	0.07	CCACGTCCAGAAGGWGACAGACTTCATGC	GTG	GAG	Nonsynonymous	Val	Glu
KLKEX4	88	A	0.66	G	0.34	0.45	CTAATGATGAGTGCRAAAAAGCCCACGTC	AAA	GAA	Nonsynonymous	Lys	Glu
KLKEX5	318	A	0.75	G	0.25	0.38	CCCCAGCTGTGTCARTCTCATGGCCTGGA	.	.	Other	5' UTR	.
MRLEX1B	156	T	0.46	C	0.54	0.50	CCGATCAGCCAATAYTGGACTTGCTGGTG	.	.	Other	5' UTR	.
MRLEX1B	16	G	0.90	C	0.10	0.18	GGGCGGGTGCCCCGCSTCCCCCCTCTGCGCG	.	.	Other	5' UTR	.
MRLEX2	1338	A	0.97	C	0.03	0.05	CTCTTTTAAAGGGAMTCCAACAGTAAACC	AAT	ACT	Nonsynonymous	Asn	Thr
MRLEX2	1405	T	0.99	C	0.01	0.03	GATGATAAAGACTAYTATTCCCTATCAGG	TAT	TAC	Synonymous	Tyr	Tyr
MRLEX2	1617	G	0.99	A	0.01	0.03	AATATCTTTATCACRATCGGCTAGAGACC	CGA	CAA	Nonsynonymous	Arg	Gln
MRLEX2	1668	A	0.97	G	0.03	0.05	CTTTCCTCCTGTCARTACTTTAGTGGAGT	AAT	AGT	Nonsynonymous	Asn	Ser
MRLEX2	1696	C	0.97	T	0.03	0.06	TCATGGAAATCACAYGGCGACCTGTCGTC	CAC	CAT	Synonymous	His	His
MRLEX2	1720	T	0.50	C	0.50	0.50	TCGTCTAGAAGAAGYGATGGGTATCCGGT	AGT	AGC	Synonymous	Ser	Ser
MRLEX9	1326	C	0.99	T	0.01	0.03	GGAATGACACACTGYGGTGTCTGCAGCTC	.	.	Other	3' UTR	.
MRLEX9	1572	A	0.43	G	0.57	0.49	GTTAAAGATCAGCTRTTCCCTTCTGATCT	.	.	Other	3' UTR	.
MRLEX9	1670	A	0.88	G	0.13	0.22	GGCCCATCTTGGCARGGTTCAGTCTGAAT	.	.	Other	3' UTR	.
MRLEX9	1964	G	0.86	A	0.14	0.24	AATCTTTTAAAAATRATGATAATCATCAG	.	.	Other	3' UTR	.
MRLEX9	247	T	0.97	C	0.03	0.06	ACCTGTTTTTAACAYGTGATGGTTGATTC	.	.	Other	3' UTR	.
MRLEX9	2551	T	0.88	C	0.13	0.22	CCAAATTGTCTGTCYGCTCTTATTTTTGT	.	.	Other	3' UTR	.
MRLEX9	2635	G	0.36	A	0.64	0.46	TCATATAATTTAAARAAACACTAAATTAG	.	.	Other	3' UTR	.
MRLEX9	869	C	0.99	G	0.01	0.02	TTTGCTGTGCTGTASATTACTGTATGTAT	.	.	Other	3' UTR	.
MRLEX9	916	A	0.83	C	0.18	0.29	AATAAGGTATAAGGMTCTTTTGTAAATGA	.	.	Other	3' UTR	.
NCX1EX12	1135	A	0.57	G	0.43	0.49	AGATTCCCAGGAACRTGCAAAATCCTTTC	.	.	Other	3' UTR	.
NCX1EX12	1190	C	0.80	T	0.20	0.32	TGATTGGCAAGGTCYTTCTTCCAGCATTC	.	.	Other	3' UTR	.
NCX1EX12	1298	A	0.99	G	0.01	0.03	ATAACCCCATTCAARAAGCACATCATCGT	.	.	Other	3' UTR	.
NCX1EX12	1366	G	0.99	C	0.01	0.03	CGTTGCTTGGGATTSTCTGTCAGTTTTAT	.	.	Other	3' UTR	.
NCX1EX12	1407	A	0.84	G	0.16	0.26	CCATGGCTTGCACARTCCTGTTCCAGTCA	.	.	Other	3' UTR	.
NCX1EX12	1841	G	0.97	C	0.03	0.06	ACCCATTAATTCAGSAAGGCCAAGGAGAA	.	.	Other	3' UTR	.
NCX1EX12	2099	T	0.94	C	0.06	0.11	GAAAGAAGCCAGGGYGACCAACGGGCCTT	.	.	Other	3' UTR	.

NCX1EX12	2123	T	0.70	Del	0.30	0.42	GCCTTTAAAAGTGTTGTCTCCTCTACTTA	.	.	Other	3' UTR	.		
NCX1EX12	2614	T	0.96	C	0.04	0.08	TGTGATTACTATTTYCATGAGTAAAAGTG	.	.	Other	3' UTR	.		
NCX1EX12	2810	G	0.67	A	0.33	0.44	TTTATCTTTGACCGRCTTGCAGATAAATA	.	.	Other	3' UTR	.		
NCX1EX12	2832	C	0.99	G	0.01	0.03	ATAAATATATCTCTSCATTTTAAACCAAG	.	.	Other	3' UTR	.		
NCX1EX12	3079	A	0.66	C	0.34	0.45	TAAACATTAGAAAAMTTTTTGCACTCATT	.	.	Other	3' UTR	.		
NCX1EX12	3193	G	0.99	C	0.01	0.03	TTGAAAGCTTTTTGSTTTGTTTGCTTTTT	.	.	Other	3' UTR	.		
NCX1EX12	664	T	0.99	C	0.01	0.03	TCTCTCCAGGTTGAYAAATCCTTAAGGCT	.	.	Other	3' UTR	.		
NCX1EX12	709	A	0.94	G	0.06	0.10	TTGGTTTTGTTTTCRGTGGAGCTGGGGAG	.	.	Other	3' UTR	.		
NCX1EX12	948	G	0.89	A	0.11	0.20	AGCATGTCTTCATCRTATTACCAAAGTTC	.	.	Other	3' UTR	.		
NCX1EX4	59	G	0.99	A	0.01	0.03	TAGAATATTTGACCRTGAGGAATATGAGA	CGT	CAT	Nonsynonymous	Arg	His		
NCX1EX9	66	A	0.97	T	0.03	0.06	ACTGACCAGCAAAGWGGAAGAGGAGAGGC	.	.	Other	Intron	.		
NETEX11	123	T	0.86	G	0.14	0.24	CGTCAGTCCTGCCTKCCTCCTGGTGTGTA	TTC	TGC	Nonsynonymous	Phe	Cys		
NETEX12	81	T	0.93	C	0.07	0.13	TCACCTACGACGACYACATCTTCCCGCCC	TAC	CAC	Nonsynonymous	Tyr	His		
NETEX13	50	G	0.93	A	0.07	0.12	GCCTATGGCATCACRCCAGAGAACGAGCA	ACG	ACA	Synonymous	Thr	Thr		
NETEX14	29	G	0.93	C	0.07	0.14	TGTCTTTCTCTGCASTTGCAACACTGGCT	.	.	Other	Intron	.		
NETEX5	121	A	0.93	C	0.07	0.12	CTCCAATGGCATCAMTGCCTACCTGCACA	AAT	ACT	Nonsynonymous	Asn	Thr		
NETEX5	175	A	0.96	G	0.04	0.07	CACGGTCAGTGCTCRGTGACCACCAAGCC	.	.	Other	Intron	.		
NETEX5	83	C	0.95	G	0.05	0.10	TTCGTGCTCCTGGTSCATGGCGTCACGCT	GTC	GTG	Synonymous	Val	Val		
NETEX7	112	G	0.92	C	0.08	0.15	TCCTTGGTTACATGSCCCATGAACACAAG	GCC	CCC	Nonsynonymous	Ala	Pro		
NETEX7	131	A	0.93	G	0.07	0.14	TGAACACAAGGTCARCATTGAGGATGTGG	AAC	AGC	Nonsynonymous	Asn	Ser		
NETEX7	73	G	0.94	C	0.06	0.11	GTATCACCAGCTTCSTCTCTGGGTTCGCC	GTC	CTC	Nonsynonymous	Val	Leu		
NETEX8	17	C	0.55	A	0.45	0.49	TGATGAGGTCCTTGMTGTTTCTTACAGGA	.	.	Other	Intron	.		
NETEX9	157	A	0.91	G	0.09	0.16	GTTCTGCATAACCARGGTGAGTAGGGGCT	AAG	AGG	Nonsynonymous	Lys	Arg		
NETEX9	56	G	0.96	A	0.04	0.07	GAGGCTGTCATCACRGGCCTGGCAGATGA	ACG	ACA	Synonymous	Thr	Thr		
NPYEX1	112	G	0.97	A	0.03	0.06	GCGCTGGCCGAGGCRTACCCCTCCAAGCC	GCG	GCA	Synonymous	Ala	Ala		
NPYEX1	178	A	0.90	G	0.10	0.18	GCCAGATACTACTCRGCGCTGGGACACTA	TCA	TCG	Synonymous	Ser	Ser		
NPYEX1	92	C	0.95	A	0.05	0.10	CCCTGCTCGTGTGCMTGGGTGCGCTGGCC	CTG	ATG	Nonsynonymous	Leu	Met		
NPYEX2	45	T	0.40	C	0.60	0.48	TATGGAAAACGATCYAGCCCAGACACT	TCT	TCC	Synonymous	Ser	Ser		
NPYEX3	100	A	0.96	G	0.04	0.08	CCTATTTTCAGCCCRTATTTCATCGTGTA	.	.	Other	3' UTR	.		
NPYEX3	78	G	0.91	T	0.09	0.16	GAGACTTGCTCTCTKGCCTTTTCCTATTT	.	.	Other	3' UTR	.		
NPYR1EX2	144	T	0.94	G	0.06	0.12	AACATACTGTCCATKTGTCTAAAATAATC			Other	5' UTR	.		

							AAA	ACA	Nonsynonymous	Lys	Thr		
NPYR1EX3	451	A	0.94	C	0.06	0.12	AGTCGCATTTAAAAMAATCAACAACAATG			Promoter			
PGISEX1	196	C	0.99	A	0.01	0.03	GCATATAATCTCTTMCTTCCTGTAAATCC	.	.	Other	Promoter	.	.
PGISEX1	396	T	0.82	G	0.18	0.30	TGCGGGGAGCAGGGKTTCTCCCAGAGCGC	.	.	Other	Promoter	.	.
PGISEX1	419	G	0.95	A	0.05	0.09	GAGCGCCCCGGTCCRACCCCTGCGGACCT	.	.	Other	5' UTR	.	.
PGISEX1	568	C	0.93	T	0.07	0.12	CCCCGCCAGCCCCGYCAGCCCCGCCAGCC	.	.	Other	Leu	Leu	.
PGISEX1	636	C	0.98	T	0.02	0.04	CACTGTTGCTGCTGYTGCTACTGAGCCGC	CTG	TTG	Synonymous	3' UTR	.	.
PGISEX10	1255	C	0.95	T	0.05	0.09	TTCTGCATTCACAGYGSCTCCTGGRCCTG	.	.	Other	Pro	Ser	.
PGISEX10	149	C	0.99	T	0.01	0.03	GCTACCGCATCCGCYCATGACACAGGGAG	CCA	TCA	Nonsynonymous	3' UTR	.	.
PGISEX10	1500	C	0.84	T	0.16	0.28	CCTGGCCAACATGGYGAAACCCCGTCTCT	.	.	Other	3' UTR	.	.
PGISEX10	1505	C	0.97	T	0.03	0.06	CCAACATGGCGAAAYCCCGTCTCTACTAA	.	.	Other	3' UTR	.	.
PGISEX10	1521	C	0.94	A	0.06	0.11	CCGTCTCTACTAAAMATAAAAAAATTAGT	.	.	Other	3' UTR	.	.
PGISEX10	1525	A	0.66	C	0.34	0.45	CTCTACTAAACATAMAAAAATTAGTCAGG	.	.	Other	3' UTR	.	.
PGISEX10	1544	G	0.65	C	0.35	0.45	ATTAGTCAGGTGTGSCGGTGCCGTGCCTG	.	.	Other	3' UTR	.	.
PGISEX10	1760	T	0.99	G	0.01	0.02	TTATGATGCTATTTKTATTAATATAAAGT	.	.	Other	3' UTR	.	.
PGISEX10	1776	C	0.99	T	0.01	0.02	ATTAATATAAAGTCYTGTTTATTGAGACC	.	.	Other	3' UTR	.	.
PGISEX10	1852	A	0.91	G	0.09	0.16	CAGCATCTCTATGARGAGAAGGAGGGTTG	.	.	Other	3' UTR	.	.
PGISEX10	2474	C	0.90	T	0.10	0.19	CGCAGGCTGCAACCYTGGTGTGCTGGGCG	.	.	Other	3' UTR	.	.
PGISEX10	2636	T	0.48	C	0.52	0.50	ACTCAAGGAAAAGAYGTGCTCCCACCAGG	.	.	Other	3' UTR	.	.
PGISEX10	270	T	0.99	C	0.01	0.03	GCTAGCATTACCACYTCCCTGCTTTTCTC	.	.	Other	3' UTR	.	.
PGISEX10	2967	C	0.98	T	0.02	0.04	TTGAGATGGAGTCTYGCTCTGCTGCCCAG	.	.	Other	3' UTR	.	.
PGISEX10	2974	C	0.52	T	0.48	0.50	GGAGTCTCGCTCTGTYGTGCCCAGGCTAGAG	.	.	Other	3' UTR	.	.
PGISEX10	3009	T	0.91	C	0.09	0.17	GGCGTGATCTCGGCYCACTGCAAGCTCTG	.	.	Other	3' UTR	.	.
PGISEX10	3022	T	0.77	C	0.23	0.35	CTCACTGCAAGCTCYGCCTCCCGTGTTCA	.	.	Other	3' UTR	.	.
PGISEX10	3061	T	0.69	C	0.31	0.43	CTGCCTCAGCCTCCYGAGTAGCTGGGACT	.	.	Other	3' UTR	.	.
PGISEX10	308	G	0.95	T	0.05	0.10	TGGGTCCAGGGGAGKGAAAAGCTAAGAGG	.	.	Other	3' UTR	.	.
PGISEX10	3082	A	0.88	G	0.12	0.21	CTGGGACTACAGGCRCCCGCCACCACACC	.	.	Other	3' UTR	.	.
PGISEX10	3139	A	0.88	G	0.13	0.22	TGGGATTTCACCGTRTTAGCCAGGATGGT	.	.	Other	3' UTR	.	.
PGISEX10	3140	T	0.82	C	0.18	0.30	GGGATTTCACCGTAYTAGCCAGGATGGTC	.	.	Other	3' UTR	.	.
PGISEX10	3186	C	0.90	T	0.10	0.17	TGATCTGCCCGCCTYGGCCTCCCAAAGTG	.	.	Other	3' UTR	.	.
PGISEX10	3214	T	0.88	C	0.12	0.21	GCTGGGATTACAGGYGTGAGCCACCGCGC	.	.	Other	3' UTR	.	.
PGISEX10	3217	G	0.88	A	0.12	0.20	GGGATTACAGGTGTRAGCCACCGCGCCCA	.	.	Other	3' UTR	.	.

PGISEX10	3244	A	0.98	C	0.02	0.04	CAGCCAAGAATAAAMTACTCTTAAGTTGA	.	.	Other	3' UTR	.	.	.	.
PGISEX10	3339	C	0.99	T	0.01	0.03	GTTTACCAAATATTYTCCTTTAAACAGAC	.	.	Other	3' UTR	.	.	.	.
PGISEX10	3419	G	0.95	A	0.05	0.10	GCCCAGGCTGGAGTRCAATGGCACGATCT	.	.	Other	3' UTR	.	.	.	.
PGISEX10	3540	A	0.98	T	0.02	0.04	CAACTGGTTTTTGTWTTTTAGTAGAGAC	.	.	Other	3' UTR	.	.	.	.
PGISEX10	3651	G	0.91	A	0.09	0.16	GATTACAGGCATGARCCACCATGCCCGGC	.	.	Other	3' UTR	.	.	.	.
PGISEX10	3663	G	0.94	A	0.06	0.11	GAGCCACCATGCCCRGCCTAAACTTTGTT	.	.	Other	3' UTR	.	.	.	.
PGISEX10	3774	C	0.85	T	0.15	0.26	ATGAAAAATAAATTYGCTGGGGAAGGGGG	.	.	Other	3' UTR	.	.	.	.
PGISEX10	3840	C	0.73	T	0.27	0.40	TCTCTGTTACAAAAYGAGATAAGCAAGTR	.	.	Other	3' UTR	.	.	.	.
PGISEX10	400	C	0.98	T	0.02	0.05	TCAGGCTTTGTCTGYTCCCAATTCACCTC	.	.	Other	3' UTR	.	.	.	.
PGISEX10	4074	A	0.96	G	0.04	0.07	GATTTTAATGATTARAAAGAATAAACACA	.	.	Other	3' UTR	.	.	.	.
PGISEX10	454	T	0.98	C	0.02	0.04	AAATGCTATTCAGAYAAGGCAGAACTAGG	.	.	Other	3' UTR	.	.	.	.
PGISEX10	573	G	0.99	T	0.01	0.02	GGATGCTGGCCACAKAAAGGCCACTCAGG	.	.	Other	3' UTR	.	.	.	.
PGISEX10	578	G	0.99	A	0.01	0.02	CTGGCCACAGAAAGRCCACTCAGGATGTC	.	.	Other	3' UTR	.	.	.	.
PGISEX10	948	C	0.99	A	0.01	0.02	CTCCTTAGACTGATMAAGCCAAAAAAGAA	.	.	Other	3' UTR	.	.	.	.
PGISEX3	165	T	0.98	A	0.02	0.05	CATTACAGCCCCAGWGATGAAAAGGCCAG	AGT	AGA	Nonsynonymous	Ser	Arg	Gly	Arg	Ser
PGISEX3	69	G	0.98	T	0.02	0.05	TCCTACGACGCGGTKGTGTGGGAGCCTCG	GTG	GTT	Synonymous	Val	Val	Val	Val	Val
PGISEX4	143	T	0.96	C	0.04	0.07	ACTTCTCCTACAGCYTCCTGCTCAGGTGA	TTC	CTC	Nonsynonymous	Phe	Leu	Ser	Leu	Phe
PGISEX4	93	A	0.99	C	0.01	0.02	GGGCGATGCTACAGMAGCAGGCAGTGGCT	GAA	GCA	Nonsynonymous	Glu	Ala	Gly	Ala	Glu
PGISEX5	79	C	0.99	T	0.01	0.02	CAGGCCCAGGACCGYGTCCACTCAGCTGA	CGC	CGT	Synonymous	Arg	Arg	Arg	Arg	Arg
PGISEX6	35	C	0.98	T	0.02	0.05	GCAGTGTCAAAAGTYGCCTGTGGAAGCTG	CGC	TGC	Nonsynonymous	Arg	Cys	Arg	Cys	Arg
PGISEX6	52	A	0.98	G	0.02	0.05	CTGTGGAAGCTGCTRTCCCCAGCCAGGCT	CTA	CTG	Synonymous	Leu	Leu	Leu	Leu	Leu
PGISEX6	97	G	0.90	A	0.10	0.18	CGGAGCAAATGGCTRGAGAGTTACCTGCT	CTG	CTA	Synonymous	Leu	Leu	Leu	Leu	Leu
PGISEX8	102	A	0.26	C	0.74	0.38	CCATGGCAGACGGGMGAGAATTCAACCTG	AGA	CGA	Synonymous	Arg	Arg	Arg	Arg	Arg
PGISEX9	42	C	0.99	T	0.01	0.02	TTCCTGAACCCTGAYGGATCAGAGAAGAA	GAC	GAT	Synonymous	Asp	Asp	Asp	Asp	Asp
PLA2AEX1	302	T	0.96	A	0.04	0.07	CCCCGCAGTCTCAAWTCGAGGTTCCCAGT	.	.	Other	Intron	.	.	.	.
PLA2AEX2	118	C	0.95	T	0.05	0.10	GGGAGTGACCCCTTYTTGGAATACAACAA	TTC	TTT	Synonymous	Phe	Phe	Phe	Phe	Phe
PLA2AEX2	42	A	0.95	C	0.05	0.10	AGTGGCCGCCGGCCGMCAGCCGGCATCAGCC	GAC	GCC	Nonsynonymous	Asp	Ala	Gly	Ala	Asp
PLA2AEX3	103	A	0.95	C	0.05	0.10	ATTTCTGCTGGACAMCCCGTACACCCACA	AAC	ACC	Nonsynonymous	Asn	Thr	Ser	Thr	Asn
PLA2AEX3	104	C	0.89	A	0.11	0.20	TTTCTGCTGGACAAMCCGTACACCCACAC	AAC	AAA	Nonsynonymous	Asn	Lys	Ser	Lys	Asn
PLA2AEX3	131	G	0.91	A	0.09	0.17	ACCTATTCATACTCRTGCTCTGGCTCGGC	TCG	TCA	Synonymous	Ser	Ser	Ser	Ser	Ser
PLA2AEX3	59	C	0.60	T	0.40	0.48	CATGACAACTGCTAYGACCAGGCCAAGAA	TAC	TAT	Synonymous	Tyr	Tyr	Tyr	Tyr	Tyr

PNMTEX3	181	A	0.89	T	0.11	0.19	GCTTGGAGGCTGTGWGCCCAGATCTTGCC	AGC	TGC	Nonsynonymous	Ser	Cys
PNMTEX3	251	T	0.89	A	0.11	0.19	GCCTGGCGGGGCACCWCCTCCTCATCGGGG	CTC	CAC	Nonsynonymous	Leu	His
PNMTEX3	269	T	0.93	A	0.08	0.14	CCTCATCGGGGCCCWGGAGGAGTCGTGGT	CTG	CAG	Nonsynonymous	Leu	Gln
PNMTEX3	380	G	0.96	A	0.04	0.08	GGTCCGGGACCTCCRCACCTATATCATGC	CGC	CAC	Nonsynonymous	Arg	His
PNMTEX3	445	T	0.96	A	0.04	0.08	GCGTCTTCTTCGCCWGGGCTCAGAAGGTT	TGG	AGG	Nonsynonymous	Trp	Arg
PNMTEX3	554	C	0.88	T	0.13	0.22	AAATAATACCCTGCYGCTGCGGTCAGTGC	.	.	Other	3' UTR	.
PNMTEX3	75	A	0.96	G	0.04	0.08	CGAGCCAGGGTGAARCGGGTCCTGCCCAT	AAA	AAG	Synonymous	Lys	Lys
PPGLUCEX1	133	G	0.98	A	0.02	0.05	CAGGTATTAAATCCRTAGTCTCGAACTAA	.	.	Other	Intron	.
PPGLUCEX1	44	C	0.99	T	0.01	0.03	ATGAAAAGCATTTAYTTTGTGGCTGGATT	TAC	TAT	Synonymous	Tyr	Tyr
PPGLUCEX1	560	C	0.99	T	0.01	0.03	AAGTACTCAAAATTYCTCTGTCCAAAGAA	.	.	Other	Intron	.
PPGLUCEX1	635	T	0.92	A	0.08	0.15	ACGTAAACTGTACAWAAATATCTCTTGGC	.	.	Other	Intron	.
PPGLUCEX2	196	G	0.93	A	0.07	0.14	AGAGGAACAGGTAARAGTCTAAGCCTGGC	.	.	Other	Intron	.
PPGLUCEX3	119	C	0.99	T	0.01	0.02	TTTGGAAGGCCAAGYTGCCAAGGAATTCA	GAT	GTT	Nonsynonymous	Ala	Val
PPGLUCEX4	447	A	0.99	T	0.01	0.02	AAATGAAACATGGGWAATGTTACATCATT	.	.	Other	3' UTR	.
PPGLUCEX4	571	C	0.96	T	0.04	0.07	TAGTGAGAACTGGAYACCGAAAAATACTT	.	.	Other	3' UTR	.
PPGLUCEX4	615	T	0.70	C	0.30	0.42	GATTTTTTAATAATYATTCATAATTGTTT	.	.	Other	3' UTR	.
PPGLUCEX4	672	T	0.98	C	0.02	0.04	AAATAATCTTTAAAYGAAAATATTTTAAG	.	.	Other	3' UTR	.
PPTHREX1	106	C	0.96	G	0.04	0.08	CCCCGGATCCCCGASCCATCCTGTGGAGC	.	.	Other	5' UTR	.
PPTHREX1	36	G	0.99	C	0.01	0.02	AGAGGGCTCGGCAGSCGCCCGGGGTCCTC	.	.	Other	5' UTR	.
PPTHREX2	19	G	0.95	A	0.05	0.09	AACCCAGACGCCGCRATGCCCCGGCCCTTG	.	.	Other	5' UTR	.
PPTHREX2	41	C	0.96	G	0.04	0.08	GCCCTTGGTTGCTGSTCGCTCTGGCTTTG	CTC	GTC	Nonsynonymous	Leu	Val
PPTHREX2	79	C	0.99	G	0.01	0.02	CTGACCGGTGTCCCSGGCGGCCGTGCTCA	CCC	CCG	Synonymous	Pro	Pro
PPTHREX3	1234	C	0.97	G	0.03	0.06	TAATGATAATAAAASCTGCATCCAGATAA	.	.	Other	3' UTR	.
PPTHREX3	185	T	0.91	C	0.09	0.16	TCATGGTCAGTCGAYGTAACCCAGCACAA	GAT	GAC	Synonymous	Asp	Asp
PPTHREX3	401	G	0.95	A	0.05	0.09	CCCTGTGGGCCCCARGGAGCCTATGGTCA	CAG	CAA	Synonymous	Gln	Gln
PPTHREX3	425	C	0.90	T	0.10	0.18	GGTCAAGCGGCCTYCTGCTGGGGCTCCT	CTC	CTT	Synonymous	Leu	Leu
PPTHREX3	512	G	0.90	A	0.10	0.19	GCAGCCTGGGTCAGRGAGCCCCTGGAGGA	AGG	AGA	Synonymous	Arg	Arg
PPTHREX3	576	A	0.91	G	0.09	0.16	CTAAGGATGTCTTGRGCCCTGTGTGCCCC	.	.	Other	3' UTR	.
PPTHREX3	895	C	0.99	A	0.01	0.03	AGCCCCTGGGAGGGMAGCCAGTGAGGGTG	.	.	Other	3' UTR	.
PPTHREX3	963	G	0.98	C	0.02	0.05	CCCCTCCCCAACCTSGCAGGATTCTCCAT	.	.	Other	3' UTR	.
PTGER3EX1	232	C	0.96	T	0.04	0.08	TGCGGCTCTCTGGAYGCCATCCCCTCCTC	.	.	Other	5' UTR	.

PTGER3EX1	371	C	0.96	G	0.04	0.07	GCGCGGGGGCAACCTSACGCGCCCTCCAGG	CTC	CTG	Synonymous	Leu	Leu
PTGER3EX1	765	A	0.98	T	0.02	0.04	GGTATGCGAGCCACWTGAAGACGCGTGCC	ATG	TTG	Nonsynonymous	Met	Leu
PTGER3EX1	878	G	0.90	T	0.10	0.18	CAGTGGCCCGGGACKTGGTGCTTCATCAG	ACG	ACT	Synonymous	Thr	Thr
PTGER3EX10	206	T	0.98	C	0.03	0.05	ACATGTTTTTGTACYTTTACTATATCTAC	.	.	Other	3' UTR	.
PTGER3EX10	281	A	0.85	G	0.15	0.26	GCGTATACATTATCRTATGTAAAATTTGC	.	.	Other	3' UTR	.
PTGER3EX2	1293	T	0.38	C	0.62	0.47	ACTAAAAATGTTTTTYCTACAGTCTACATG	.	.	Other	Intron	.
PTGER3EX2	1295	T	0.86	C	0.14	0.23	TAAAATGTTTTTTCYACAGTCTACATGAA	.	.	Other	Intron	.
PTGER3EX2	1393	T	0.84	C	0.16	0.27	GCACTTCTTAAAAAYGTCTCCCCACCAAA	.	.	Other	Intron	.
PTGER3EX2	1403	C	0.98	A	0.03	0.05	AAAATGTCTCCCCAMCAAACATAGTAATC	.	.	Other	Intron	.
PTGER3EX2	1614	T	0.94	C	0.06	0.11	TAAAGAATTAATTTYGATAGGTACAATAT	.	.	Other	Intron	.
PTGER3EX2	1719	G	0.98	C	0.03	0.05	TGGAGACAAAATCTSTTGAGAGTGCTTAT	.	.	Other	Intron	.
PTGER3EX2	2153	A	0.99	G	0.01	0.03	AGTCCATCAGGCTGRTAAAGTGAATTATT	.	.	Other	Intron	.
PTGER3EX2	2517	T	0.92	C	0.08	0.15	TAGGCATTCGTTAGYATGGGGAAACCTGA	.	.	Other	Intron	.
PTGER3EX2	3069	T	0.93	C	0.08	0.14	TAGTGCTGTATATAYCCCAAGATATTTTA	.	.	Other	Intron	.
PTGER3EX2	3101	A	0.91	G	0.09	0.17	AAATGTAAGTGTTTRATCATGCCAGATTT	.	.	Other	Intron	.
PTGER3EX2	326	T	0.91	A	0.09	0.17	ATATCGCTAAACCTWACTGTGAATTTAGG	.	.	Other	Intron	.
PTGER3EX2	3282	A	0.98	G	0.03	0.05	ACTAAAAACTGGCARACAGTATTTTAATA	.	.	Other	Intron	.
PTGER3EX2	3382	T	0.63	C	0.37	0.47	TTTTTATAATTTTGYTCTTTTTGACTCCA	.	.	Other	Intron	.
PTGER3EX2	557	G	0.99	T	0.01	0.03	TATAAATGATCTTGKTCTATTGGGGAGCG	.	.	Other	Intron	.
PTGER3EX2	628	T	0.83	C	0.17	0.28	AACCACATACATCAYTGAAGACAAGGGAT	.	.	Other	Intron	.
PTGER3EX2	769	T	0.91	A	0.09	0.17	GTATAATGTATTTAWAATATTCATCGATA	.	.	Other	Intron	.
PTGER3EX2	787	T	0.94	G	0.06	0.12	ATTCATCGATACCAKTATTCAAATATTGC	.	.	Other	Intron	.
PTGER3EX2	805	A	0.91	C	0.09	0.16	TCAAATATTGCTCAMTACAGCAAATTAGC	.	.	Other	Intron	.
PTGER3EX2	850	G	0.98	A	0.02	0.04	TTTAAGTTTACTTGRATTGATAATTAGGT	.	.	Other	Intron	.
PTGER3EX2	852	T	0.62	A	0.38	0.47	TAAGTTTACTTGGAWTGATAATTAGGTTT	.	.	Other	Intron	.
PTGER3EX2	855	A	0.98	T	0.02	0.04	GTTTACTTGGATTGWTAATTAGGTTTACT	.	.	Other	Intron	.
PTGER3EX3	76	C	0.94	T	0.06	0.12	CTCCACCTCCTTACYCTGCCAGTGTTCCT	CCC	CTC	Nonsynonymous	Pro	Leu
PTGER3EX3	80	C	0.93	T	0.07	0.13	ACCTCCTTACCCTGYCAGTGTTCCTCAAC	TGC	TGT	Synonymous	Cys	Cys
PTGER3EX4	719	G	0.84	T	0.16	0.27	TCTAAGCTTTTGATKACAAAGGAGTGATG	.	.	Other	3' UTR	.
PTGER3EX4	94	C	0.98	T	0.03	0.05	TTTGCATATTTCTTYCCACCTGAGAAGGA	.	.	Other	3' UTR	.
PTGER3EX6	197	A	0.98	G	0.03	0.05	GAGTGCTGTGTTTTRAAAAGCAAGCTCC	.	.	Other	3' UTR	.

PTGER3EX6	300	G	0.91	A	0.09	0.16	GAGATTACCAGCAARCCAGGTCATTTCCG	.	.	Other	3' UTR	.	.	.	.
PTGER3EX6	387	T	0.98	A	0.03	0.05	CCAATTTAGACTTAWAGTAAGAATAGCAC	.	.	Other	3' UTR	.	.	.	.
PTGER3EX7	85	A	0.98	G	0.02	0.04	TTGGTGCAGTTCTCRTGATAGTGAGTGAG	CAT	CGT	Nonsynonymous	His	Arg	.	.	.
PTGER3EX8	116	C	0.83	T	0.17	0.28	GATTTGTCCTTTCCYGCCATGTCTTCATC	CCC	CCT	Synonymous	Pro	Pro	.	.	.
PTGER3EX9	16	T	0.94	C	0.06	0.12	TGCCTATCACATAAYAGGAGAACCCTGCA	.	.	Other	Intron	.	.	.	.
RENEX1	80	A		T			GGAAGCATGGATGGWTGGAGAAGGATGCC	GGA	GGT	Synonymous	Gly	Gly	.	.	.
RENEX2	135	A	0.76	C	0.24	0.37	ATGAAGAGGCTGACMCTTGGCAACACCAC	ACA	ACC	Synonymous	Thr	Thr	.	.	.
RENEX4	151	A	0.97	G	0.03	0.05	GACATCATCACCGTRAGTTGGGCCGCCCT	.	.	Other	Intron	.	.	.	.
RENEX4	165	T	0.66	G	0.34	0.45	AAGTTGGGCCGCCCKAGGTCATCTGCCCC	.	.	Other	Intron	.	.	.	.
RENEX9	138	G	0.99	A	0.01	0.03	TTCAGGTGAGGTTCRAGTCGGCCCCCTCG	.	.	Other	Intron	.	.	.	.
SAEX1	167	T	0.91	C	0.09	0.17	GTTTTGGGCCAGTCYTGCTCCTCCGGATT	.	.	Other	Promoter	.	.	.	.
SAEX1	76	G	0.98	T	0.03	0.05	ATTACCTGTAAGAGKAACCGCTGGGAGTC	.	.	Other	Promoter	.	.	.	.
SAEX11	143	C	0.99	T	0.01	0.02	AGAGCAGATGATGTYATATTATCCTCTGG	GTC	GTT	Synonymous	Val	Val	.	.	.
SAEX2	54	T	0.94	C	0.06	0.12	CTCTGTGCAAATCCYGAGTGCTAAAGCTT	.	.	Other	5' UTR	.	.	.	.
SAEX3	109	T	0.99	C	0.01	0.03	GAGTTTTGAGGAACYGGGATCTCTGTCCA	CTG	CCG	Nonsynonymous	Leu	Pro	.	.	.
SAEX4	187	T	0.82	C	0.18	0.30	CACTCCAAGCTGATYGTATCAGAGAACTC	ATT	ATC	Synonymous	Ile	Ile	.	.	.
SAEX5	182	T	0.14	C	0.86	0.24	TGGAAGGTATACTTYCACAAAAGTGCAGC	.	.	Other	Intron	.	.	.	.
SAEX8	111	G	0.97	C	0.03	0.06	AAATGGAGAAACAASACGGGCCTGGATAT	AAG	AAC	Nonsynonymous	Lys	Asn	.	.	.
SAEX9	101	C	0.98	T	0.03	0.05	CCTTCTCCTGCTTTYGATGTTAAGGTTTG	TTC	TTT	Synonymous	Phe	Phe	.	.	.
SCNN1GEX1	167	G	0.48	A	0.52	0.50	GGTGGCCCAGGAAGRCGCAGCGCGGCCGG	.	.	Other	Promoter	.	.	.	.
SCNN1GEX1	236	G	0.81	T	0.19	0.30	TGAAGTCGTGGCCCKCTCCGGGCGGTCTC	.	.	Other	Promoter	.	.	.	.
SCNN1GEX1	498	G	0.99	A	0.01	0.02	TGGAGCGGATGCCGRGCGCCAGGGCGTCG	.	.	Other	Intron	.	.	.	.
SCNN1GEX1	552	C	0.70	G	0.30	0.42	GAGCCAGCATCAGCSGGTGGCGGCTTCCC	.	.	Other	Intron	.	.	.	.
SCNN1GEX1	553	G	0.99	A	0.01	0.02	AGCCAGCATCAGCCRGTGGCGGCTTCCCG	.	.	Other	Intron	.	.	.	.
SCNN1GEX12	1016	T	0.80	A	0.20	0.32	AGATCAGAGTGCCGWGGTGGAGGTCTGGG	.	.	Other	3' UTR	.	.	.	.
SCNN1GEX12	1085	A	0.75	G	0.25	0.38	CAGGAGATGGATTTRGTTATTCAATTTTG	.	.	Other	3' UTR	.	.	.	.
SCNN1GEX12	407	C	0.78	G	0.22	0.34	ATGCTGGATGAGCTSTGAGGCAGGGTTGA	CTC	CTG	Synonymous	Leu	Leu	.	.	.
SCNN1GEX12	454	G	0.99	T	0.01	0.02	GACCACCAGCCATGKTCTAAGGACATGGA	.	.	Other	3' UTR	.	.	.	.
SCNN1GEX12	485	G	0.99	A	0.01	0.02	GGGTGCCCCCAGACRTGTGCACAGGGGAC	.	.	Other	3' UTR	.	.	.	.
SCNN1GEX12	569	T	0.86	G	0.14	0.24	CGCAAGATGGGGCCKGGGCATGCGCAGGA	.	.	Other	3' UTR	.	.	.	.
SCNN1GEX12	646	C	0.80	T	0.20	0.32	ATAAATCCCGGGACYTGAACTATTAGCAC	.	.	Other	3' UTR	.	.	.	.

SCN1GEX12	678	G	0.80	A	0.20	0.32	ACTAGAGACTGGGARCCGAGGCAGTGGTG	.	.	Other	3' UTR	.
SCN1GEX12	982	A	0.76	G	0.24	0.37	GAGAACTGGCCCAGRGCCCTTGGAGTGTT	.	.	Other	3' UTR	.
SCN1GEX2	219	G	0.92	T	0.08	0.14	TCGTGGTGTCCCGCKGCCGTCTGCGCCGC	GGC	TGC	Nonsynonymous	Gly	Cys
SCN1GEX2	26	G	0.16	C	0.84	0.27	TCTTCTTTGCCCCTSCAGCACGCCCGTCC	.	.	Other	Intron	.
SCN1GEX2	43	G	0.36	A	0.64	0.46	GCACGCCCGTCCTCRGAGTCCCGTCCTCA	.	.	Other	5' UTR	.
SCN1GEX3	186	T	0.79	C	0.21	0.34	TTCTCCCACCGGATYCCGCTGCTGATCTT	ATT	ATC	Synonymous	Ile	Ile
SCN1GEX3	259	G	0.94	A	0.06	0.12	GGAAGCGGAAAGTCRGCGGTAGCATCATT	GGC	AGC	Nonsynonymous	Gly	Ser
SCN1GEX3	261	C	0.91	T	0.09	0.16	AAGCGGAAAGTCGGYGGTAGCATCATTCA	GGC	GGT	Synonymous	Gly	Gly
SCN1GEX3	301	G	0.97	A	0.03	0.06	ATGTCATGCACATCRAGTCCAAGCAAGTG	GAG	AAG	Nonsynonymous	Glu	Lys
SCN1GEX3	99	T	0.73	C	0.27	0.40	CTGAAGTCCCTGTAYGGCTTTCCAGAGTC	TAT	TAC	Synonymous	Tyr	Tyr
SCN1GEX4	47	C	0.96	T	0.04	0.07	TCAAATGACACCTCYGACTGTGCCACCTA	TCC	TCT	Synonymous	Ser	Ser
SCN1GEX7	142	G	0.70	A	0.30	0.42	GGTAACAGATTGGCRGGGGCACCCAGCCC	.	.	Other	Intron	.
TBXA2REX1	518	T	0.89	A	0.11	0.20	GCTGGGCCCGCCCCWGGTCACAGCCAGAC	.	.	Other	5' UTR	.
TBXA2REX1B	130	T	0.80	C	0.20	0.32	CTCAGCCTCCCGAGYAGCTGGGATTACAG	.	.	Other	5' UTR	.
TBXA2REX2	292	T	0.98	A	0.02	0.04	TCCTCACCTTCCTCWGCGGCCTCGTCCTC	TGC	AGC	Nonsynonymous	Cys	Ser
TBXA2REX2	329	T	0.98	A	0.03	0.05	CCTGGGGCTGCTGGWGACCGGTACCATCG	GTG	GAG	Nonsynonymous	Val	Glu
TBXA2REX2	333	C	0.96	T	0.04	0.08	GGGCTGCTGGTGACYGGTACCATCGTGGT	ACC	ACT	Synonymous	Thr	Thr
TBXA2REX2	371	A	0.99	T	0.01	0.03	CGCCGCGCTCTTCGWGTGGCACGCCGTGG	GAG	GTG	Nonsynonymous	Glu	Val
TBXA2REX2	390	T	0.94	A	0.06	0.12	CACGCCGTGGACCCWGGCTGCCGTCTCTG	CCT	CCA	Synonymous	Pro	Pro
TBXA2REX2	525	G	0.95	A	0.05	0.10	CCGGCGGTCGCCTCRCAGCGCCGCGCCTG	TCG	TCA	Synonymous	Ser	Ser
TBXA2REX2	568	G	0.99	A	0.01	0.02	TGGTGTGGAGCGGCCRCGCTGGCGCTGGGC	GCG	ACG	Nonsynonymous	Ala	Thr
TBXA2REX2	617	T	0.98	A	0.03	0.05	GGGTCGCTACACCGWGCAATACCCGGGGT	GTG	GAG	Nonsynonymous	Val	Glu
TBXA2REX2	739	G	0.96	A	0.04	0.07	TCCTGCTGAACACGRTCAGCGTGGCCACC	GTC	ATC	Nonsynonymous	Val	Ile
TBXA2REX2	852	C	0.98	A	0.02	0.04	ATCATGGTGGTGGCMAGCGTGTGTTGGCT	GCC	GCA	Synonymous	Ala	Ala
TBXA2REX3	145	T	0.36	C	0.64	0.46	GACCCCTGGGTGTAYATCCTGTTCCGCCG	TAT	TAC	Synonymous	Tyr	Tyr
TBXA2REX3	358	A	0.93	G	0.07	0.13	GGGGTGCTGGATGGRCAGTGGGCATCAGC	.	.	Other	3' UTR	.
TBXA2REX3	528	A	0.89	G	0.11	0.19	AAGGGCATGCAGACRTTGGAAGAGGGTCT	.	.	Other	3' UTR	.
TBXA2REX3	599	C	0.89	T	0.11	0.20	CCCAGGCTGGAGTGYAGTGGCGCAATCTC	.	.	Other	3' UTR	.
TBXA2REX3	701	C	0.86	T	0.14	0.24	GGCGCGCGCCACCAYGCCCGGCTAATTTT	.	.	Other	3' UTR	.
TBXA2REX3	904	A	0.70	G	0.30	0.42	TGGAGTACAGTGGCRCGATCTCGGCTCAC	.	.	Other	3' UTR	.
TBXA2REX3	906	G	0.53	A	0.47	0.50	GAGTACAGTGGCACRATCTCGGCTCACTG	.	.	Other	3' UTR	.

TBXA2REX3	953	G	0.39	C	0.61	0.47	TTCAAGCGATTCTCSTGCCTCAGCCTCCC	.	.	Other	3' UTR	.
TBXASEX10	61	G	0.97	T	0.03	0.06	CAGCCTCGAGGAAGKCCTGCCCTATCTGG	GGC	GTC	Nonsynonymous	Gly	Val
TBXASEX10	98	G	0.93	A	0.07	0.14	ATTGCAGAGACGCTRAGGATGTACCCGCC	CTG	CTA	Synonymous	Leu	Leu
TBXASEX11	105	C	0.91	T	0.09	0.16	GTGCTAGAGATGGCYGTGGGTGCCCTGCA	GCC	GCT	Synonymous	Ala	Ala
TBXASEX11	152	C	0.99	A	0.01	0.03	GCCAAGCCCGGAGAMCTTCAACCCTGAAA	ACC	AAC	Nonsynonymous	Thr	Asn
TBXASEX11	49	C	0.98	G	0.02	0.05	CACGGGAGGCAGCTSAGGACTGCGAGGTG	CAG	GAG	Synonymous	Gln	Glu
TBXASEX11	73	C	0.99	T	0.01	0.02	AGGTGCTGGGGCAGYGCATCCCCGCAGGC	CGC	TGC	Nonsynonymous	Arg	Cys
TBXASEX11	88	G	0.90	A	0.10	0.18	GCATCCCCGCAGGCRCTGTGCTAGAGATG	GCT	ACT	Nonsynonymous	Ala	Thr
TBXASEX12	46	C	0.98	A	0.02	0.04	TCACGGCTGAGGCCMGGCAGCAGCACCGG	CGG	AGG	Synonymous	Arg	Arg
TBXASEX13	226	A	0.99	G	0.01	0.02	CCTGGCATGCAAGGRTAAGAGGTTCTTTT	.	.	Other	3' UTR	.
TBXASEX4	130	C	0.99	T	0.01	0.03	CCAACAGAATGGTAYGTAGTTTTCTTTCC	.	.	Other	Intron	.
TBXASEX5	15	G	0.99	A	0.01	0.02	CTGACCCTCTGCTTRTTACTTCCCAACAG	.	.	Other	Intron	.
TBXASEX6	59	C	0.98	A	0.02	0.04	AGCCAAGCCTGCGAMCTTCTCCTGGCTCA	GAC	GAA	Synonymous	Asp	Asp
TBXASEX8	110	A	0.89	G	0.11	0.20	ATGGCTTTTTTAACRAACTCATTAGGAAT	AAA	GAA	Nonsynonymous	Lys	Asp
TBXASEX8	119	A	0.99	G	0.01	0.03	TTAACAAACTCATTRGGAATGTGATTGCC	AGG	GGG	Nonsynonymous	Arg	Gly
TBXASEX9	156	C	0.96	A	0.04	0.07	CGAACCCTTCCCGGMAACACCAGCCCAGC	CAA	AAA	Nonsynonymous	Gln	Lys
TBXASEX9	276	C	0.88	G	0.12	0.21	CTTTTGCCACCTACSTACTGGCCACCAAC	CTA	GTA	Nonsynonymous	Leu	Val
TRHREX1	56	G	0.44	C	0.56	0.49	TTCTGCAGAACTTASATGATAAGCAACGA	.	.	Other	Promoter	.
TRHREX1	84	T	0.98	C	0.02	0.04	ACAAAGCCAGCTGCYTCTAGACCCCTGGC	.	.	Other	Promoter	.
TRHREX2	147	C	0.99	A	0.01	0.03	GTCAGTGAACTGAAMCAAACACAGCTTCA	AAC	AAA	Nonsynonymous	Asn	Lys
TRHREX2	240	A	0.99	G	0.01	0.03	GGCCTGGGCATTGTRGGCAACATCATGGT	GTA	GTG	Synonymous	Val	Val
TRHREX3	1161	T	0.58	C	0.42	0.49	TCCCACATGATGGGYGGAAAAAGGCAAAA	.	.	Other	3' UTR	.
TRHREX3	1231	T	0.98	C	0.03	0.05	TTAAATTTGAAAAGYATAGTCAAGACAAA	.	.	Other	3' UTR	.
TRHREX3	1540	T	0.97	A	0.03	0.06	TTCTTTTTTTGTTTWTCTCAAATGCTAGT	.	.	Other	3' UTR	.
TRHREX3	1786	A	0.99	T	0.01	0.03	GAATCTCCGAGGGCWAAAATTGCCCTTGG	.	.	Other	3' UTR	.
TRHREX3	1846	T	0.94	C	0.06	0.12	GTAGATCAAAAAAGYACCCATACCTTTAC	.	.	Other	3' UTR	.
TRHREX3	2046	G	0.98	A	0.02	0.04	CCTCATTCTAGAGTRCGCTTTTTTTTTTT	.	.	Other	3' UTR	.
TRHREX3	2175	A	0.97	G	0.03	0.06	ACCTGCATGACAGTRAGCAATCTATGTTA	.	.	Other	3' UTR	.
TRHREX3	2283	G	0.95	A	0.05	0.10	ACAAGCACATGTGTRTTTATAAACACATA	.	.	Other	3' UTR	.
TRHREX3	377	T	0.95	C	0.05	0.10	GCCACAAAAGTGTCYTTTGATGACACCTG	TCT	TCC	Synonymous	Ser	Ser
TRHREX3	960	T	0.96	C	0.04	0.07	TAAGATTTTAGACAYACATGTTAACTGTA	.	.	Other	3' UTR	.

TABLE 2

Gene/ExOn	Base Position	Ref Allele	Freq (P)	Alt Allele	Freq (Q)	Hetero-zygosity (H)	Sequence Tag	Ref Codon	Alt Codon	Type of amino acid change	Ref amino acid	Alt amino acid
ACEEX13	138	C	0.81	T	0.19	0.30	CCTCTGCTGGTCCCYAGCCAGGAGGCATC	CCC	CCT	Synonymous	Pro	Pro
ACEEX17	52	A	0.20	G	0.80	0.32	AATGTGATGGCYACRTCCCGGAAATATGA	ACA	ACG	Synonymous	Thr	Thr
ADRB3EX1	416	T	0.90	C	0.10	0.18	TCGTGGCCATCGCCYGGACTCCGAGACTC	TGG	CGC	Nonsynonymous	Trp	Arg
AGTEX2	644	C	0.86	T	0.14	0.24	GCTGCTGCTGTCCAYGGTGGTGGGCGTGT	ACG	ATG	Nonsynonymous	Thr	Met
AGTEX2	827	T	0.10	C	0.90	0.18	TGGCTGCTCCCTGAYGGGAGCCAGTGTGG	ATG	ACT	Nonsynonymous	Met	Thr
AGTEXP1	173	C	0.71	T	0.29	0.41	TGCTTGTGTGTTTTYCCCAGTGTCTATTA	.	.	Other	Promoter	.
AGTEXP2	203	G	0.86	A	0.14	0.24	CTCGACCCTGCACCRGCTCACTCTGTTCA	.	.	Other	Promoter	.
AGTEXP3	144	C	0.24	A	0.76	0.37	GCTATAAATAGGGCMTCGTGACCCGGCCA	.	.	Other	Promoter	.
ANPEX3	120	T	0.91	C	0.09	0.16	GTCTCTGCTGCATTYGTGTCATCTTGTTG	.	.	Other	3'UTR	.
ANPEX3	33	T	0.80	C	0.20	0.32	TCTCTTTGCAGTACYGAAGATAACAGCCA	TGA	AGA	Nonsynonymous	Stop	Arg
AT1EX5	1138	A	0.93	G	0.07	0.13	AAGAAGCCTGCACCRTGTTTTGAGGTTGA	CCA	CCG	Synonymous	Pro	Pro
AT1EX5	1593	G	0.88	T	0.12	0.21	AAAGTTTTCGTGCCKGTTTTCAGCTATTA	.	.	Other	3'UTR	.
AT1EX5	649	T	0.61	C	0.39	0.47	CAAAATTCAACCCTYCCGATAGGGCTGGG	CTT	CTC	Synonymous	Leu	Leu
MRLEX2	1504	C	0.89	T	0.11	0.20	CAAGAACCAGATGAYGGGAGCTATTACCC	GAC	GAT	Synonymous	Asp	Asp
MRLEX2	545	A	0.81	G	0.19	0.30	GCGTCATGCGCGCCRTTGTTAAAAGCCCT	ATT	GTT	Nonsynonymous	Ile	Val
NCXIEX12	3101	A	0.16	T	0.84	0.26	ACTCATTTTTTAGCWGTATTAGGAATGTC	.	.	Other	3'UTR	.

Table 3

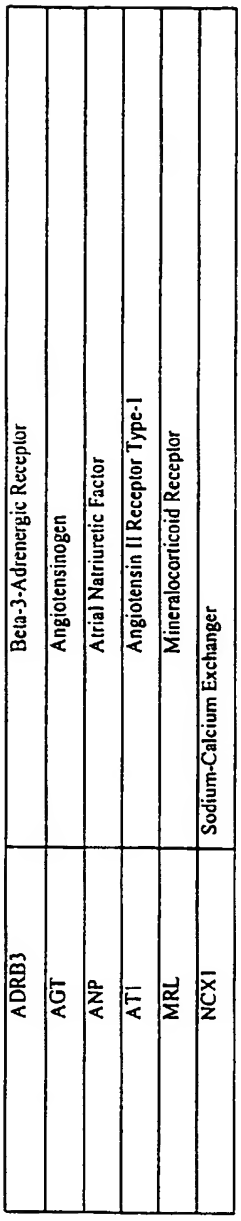
Gene/Exon	Gene Name
Table 1	
AADD	Alpha-Adducin
ACE	Angiotensin Converting Enzyme
ADDB	Beta Adducin
ADDG	Gamma Adducin
ADORA2A	A2a Adenosine Receptor
ADRB3	Beta-3-Adrenergic Receptor
ADROM	(prepro)Adrenomedullin
AE1	Anion Exchanger
AGT	Angiotensinogen
ALDRED	Aldose Reductase
ANPEX1	Atrial Natriuretic Factor
APOA1	Apolipoprotein A-I
APOA2	Apolipoprotein A-II
APOA4	Apolipoprotein A-IV
APOC1EX1	Apolipoprotein C-I
APOC2	Apolipoprotein C-II
APOC3	Apolipoprotein C-III
APOC4	Apolipoprotein C-IV
APOER2	Apolipoprotein E Receptor 2
AT1	Angiotensin II Receptor Type-I
AT2	Angiotensin II Receptor Type 2
AVP	Arginine Vasopressin
AVPR2	Arginine Vasopressin Receptor Type II
BIR	Beta Inward Rectifier Subunit (Pancreatic K Channel)
BKRB2	B2-Bradykinin Receptor
BNP	Brain Natriuretic Protein

BRS3	Bombesin Receptor Subtype-3
CAL/CGRP	Calcitonin/Calcitonin Gene Related Peptide
CHY	Chymase
CLCNKB	Chloride Channel (Human Kidney - B)
CNP	C-Type Natriuretic Peptide
COX1	Cyclooxygenase -1
COX2	Cyclooxygenase -2
CYP11B1	Cytochrome P-450 11 Beta 1
CYP11B2	Cytochrome P-450 11 Beta 2
DBH	Dopamine Beta-Hydroxylase
DD1R	Dopamine D1 Receptor
EDNRA	Endothelin Receptor Subtype A
EDNRB	Endothelin Receptor Subtype B
ELAM1	Endothelial Leukocyte Adhesion Molecule 1
ENDOTHEL	Endothelin-2
ET1	Endothelin-1
GALNR	Galanin Receptor
GGR	Glucagon Receptor
GH1	Growth Hormone 1
GH2	Growth Hormone 2
GIPR	Glucose Insulinotropic Peptide Receptor or Gastric Inhibitory Polypeptide Receptor
GLUT2	Glucose Transporter 2
GLUT4	Glucose Transporter 4
GLUT5	Glucose Transport-Like 5
GNB3	G-Protein Beta-3 Chain
GSY1	Glycogen Synthetase
HAPT	Haptoglobin
HSD11K	Hydroxysteroid Dehydrogenase 11 Beta Kidney Isozyme
HSTSCGENE	Homo sapiens Thiazide-Sensitive Cotransporter

HUMAPNHA	Human Na/H Antiporter
HUMGFAT	Human Glutamine:Fructose-6-Phosphate Amidotransferase
HUMGLTRN	Human Glucose Transporter
HUMGUANCYC	Human Guanylate Cyclase
IAPP	Islet Amyloid Polypeptide
ICAM1	Intercellular Adhesion Molecule 1
ICAM2	Intercellular Adhesion Molecule 2
INS	Insulin
KALST	Kallistatin
KLK	Kallikrein
MRL	Mineralocorticoid Receptor
NCX1	Sodium-Calcium Exchanger
NET	Norepinephrine Transporter
NPY	Neuropeptide Y
NPYR1	Neuropeptide Y Y1 Receptor
PGIS	Prostacyclin Synthase
PLA2A	Pancreatic Phospholipase A-2
PNMT	Phenylethanolamine N-Methyltransferase
PPGLUC	Preproglucagon
PPTHR	Preprothyrotropin-Releasing Hormone
PTGER3	Prostaglandin E Receptor EP3 Subtype
REN	Renin
SA	SA Gene Acetyl-CoA Synthetase Homologue ?? (a candidate gene for genetic hypertension)
SCNN1G	Amiloride-Sensitive Epithelial Sodium Channel Gamma Subunit
TBXA2R	Thromboxane A2 Receptor
TBXAS0	Thromboxane Synthase
TRHR	Thyrotropin-Releasing Hormone Receptor

Table 2

ACE	Angiotensin Converting Enzyme



ADRB3	Beta-3-Adrenergic Receptor
AGT	Angiotensinogen
ANP	Atrial Natriuretic Factor
ATI	Angiotensin II Receptor Type-1
MRL	Mineralocorticoid Receptor
NCX1	Sodium-Calcium Exchanger

Claims

1. A nucleic acid of between 10 and 100 bases comprising at least 10 contiguous nucleotides including a polymorphic site from a sequence shown in Table 1, column 8 or the complement thereof.

2. The nucleic acid of claim 1 that is DNA.

3. The nucleic acid of claim 1 that is RNA.

4. The nucleic acid of claim 1 that is less than 50 bases.

5. The nucleic acid of claim 1 that is less than 20 bases.

6. The nucleic acid of claim 1, wherein the polymorphic form occupying the polymorphic site is a reference base shown in Table 1, column 3.

7. The nucleic acid of claim 1, wherein the polymorphic form occupying the polymorphic site is an altemative base shown in Table 1, column 5.

8. The nucleic acid of claim 7, wherein the alternative base correlates with hypertension or susceptibility thereto.

9. The nucleic acid of claim 1, wherein the polymorphic site is one for which reference and altemative bases shown in columns 3 and 5 of Table 1 are respectively components of different codons encoding different amino acids.

10. The nucleic acid of claim 1, which is from a gene encoding a human angiotensin I receptor.

11. The nucleic acid of claim 1, which is from a gene encoding an angiotensin II receptor.

12. The nucleic acid of claim 1, which is from a gene encoding an atrial natriuretic peptide.

13. The nucleic acid of claim 1, which is from a gene encoding a β-3-adrenergic receptor.

14. The nucleic acid of claim 1, which is from a gene encoding a bradykinin receptor B2.

15. The nucleic acid of claim 1, which is from a gene encoding a mineralocorticoid receptor

16. The nucleic acid of claim 1, which is from a gene encoding a renin protein.

17. The nucleic acid of claim 1, which from a gene encoding an angiotensinogen protein.

18. The nucleic acid of claim 1, which from a gene encoding a sodium calcium ion channel.

19. The nucleic acid of claim 1, which is from a gene encoding an angiotensin converting protein.

20. The nucleic acid of claim 1, which is from a gene encoding an angiotensin converting protein.

21. Allele-specific oligonucleotide that hybridizes to a sequence including a polymorphic site shown in Table 1 or the complement thereof.

22. The allele-specific oligonucleotide of claim 21 that is a probe.

23. An isolated nucleic acid comprising a sequence of Table 1, column 8 or the complement thereof, wherein the polymorphic site within the sequence or its complement is occupied by a base other than the reference base show in Table 1, column 3.

24. A method of analyzing a nucleic acid, comprising:

obtaining the nucleic acid from an individual; and
determining a base occupying any one of the polymorphic sites shown in Table 1 or other polymorphic sites in equilibrium dislinkage therewith.

25. The method of claim 24, wherein the determining comprises determining a set of bases occupying a set of the polymorphic sites shown in Table 1.

26. The method of claim 25, wherein the nucleic acid is obtained from a plurality of individuals, and a base occupying one of the polymorphic positions is determined in each of the individuals, and the method further comprising testing each individual for the presence of a disease phenotype, and correlating the presence of the disease phenotype with the base.

27. The method of claim 24, wherein the determined base is correlated with susceptibility to hypertension.

28. A method of diagnosing a phenotype comprising:

determining which polymorphic form(s) are present in a sample from a subject at one or more polymorphic sites shown in Table 1;
diagnosing the presence of a phenotype correlated with the form(s) in the subject.

29. The method of claim 28, wherein the phenotype is hypertension.

30. A method of screening for a polymorphic site suitable for diagnosing a phenotype, comprising:

identifying a polymorphic site linked to a polymorphic site shown in Table 1, wherein a polymorphic form of the polymorphic site shown in Table 1 has been correlated with a phenotype; and
determining haplotypes in a population of individuals to indicate whether the linked polymorphic site has a polymorphic form in equlibrium dislinkage with the polymorphic form correlated with the phenotype.

31. The method of claim 30, wherein the polymorphic form of the polymorphic site shown in Table 1 has been correlated with hypertension.

32. The method of claim 30, wherein the linked polymorphic site and the polymorphic site shown in Table 1 are from the same gene.

33. A computer-readable storage medium for storing data for access by an application program being executed on a data processing system, comprising:

a data structure stored in the computer-readable storage medium, the data structure including information resident in a database used by the application program and including:
a plurality of records, each record of the plurality comprising information identifying a polymorphisms shown in Table 1.

34. The computer-readable storage medium of claim33, wherein each record has a field identifying a base occupying a polymorphic site and a location of the polymorphic site.

35. The computer-readable storage medium of claim 33, wherein each record identifies a nucleic acid segment of between 10 and 100 bases from a fragment shown in Table 1 including a polymorphic site, or the complement of the segment.

36. The computer-readable storage medium of claim 33, comprising at least 10 records, each record comprising information identifying a different polymorphism shown in Table 1.

37. The computer-readable storage medium of claim33, comprising at least 10 records, each record comprising information identifying a different polymorphism shown in Table 1.

38. A signal carrying data for access by an application program being executed on a data processing system, comprising:

a data structure encoded in the signal, said data structure including information resident in a database used by the application program and including:
a plurality of records, each record of the plurality comprising information identifying a polymorphism shown in Table 1

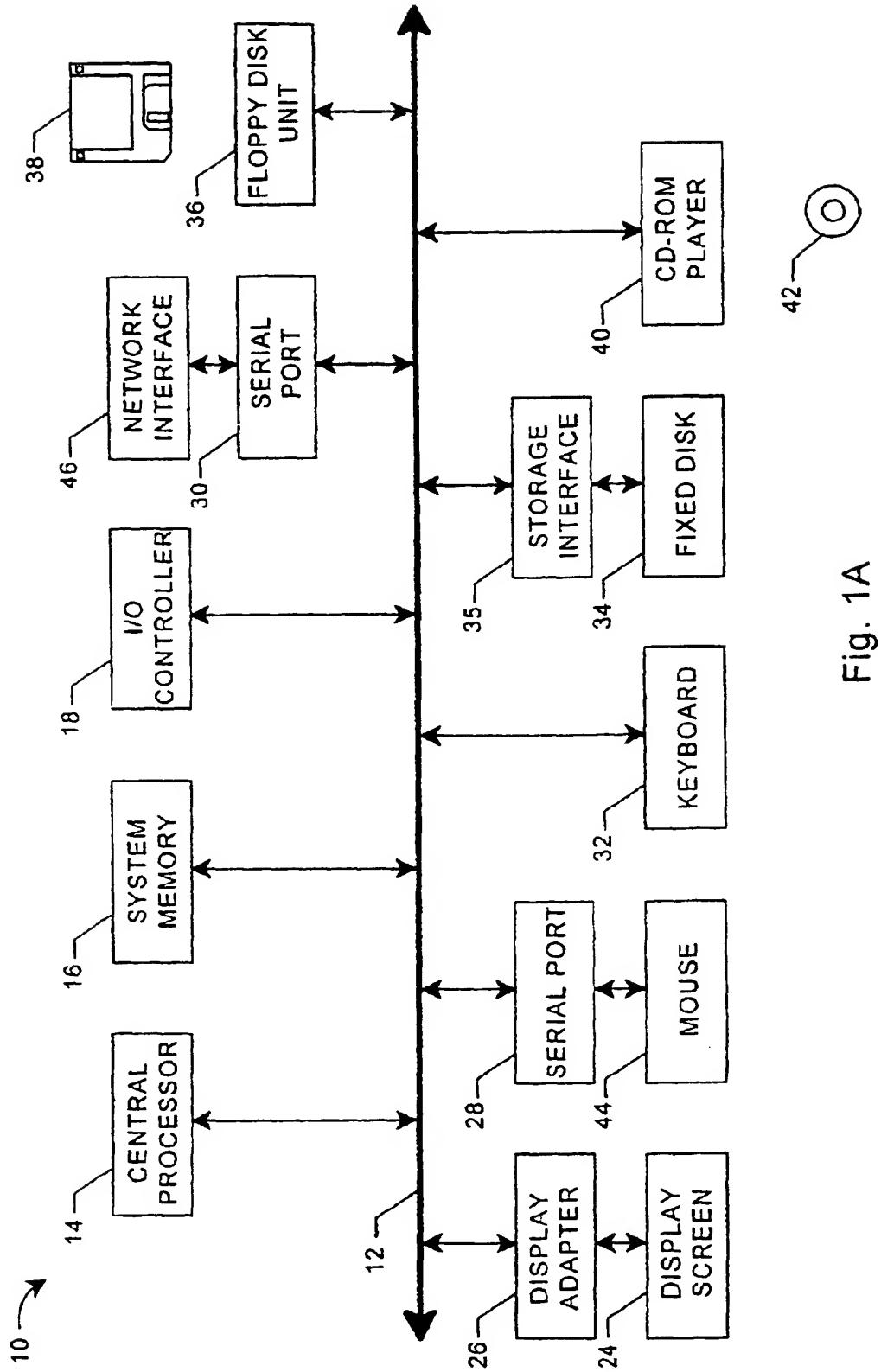


Fig. 1A

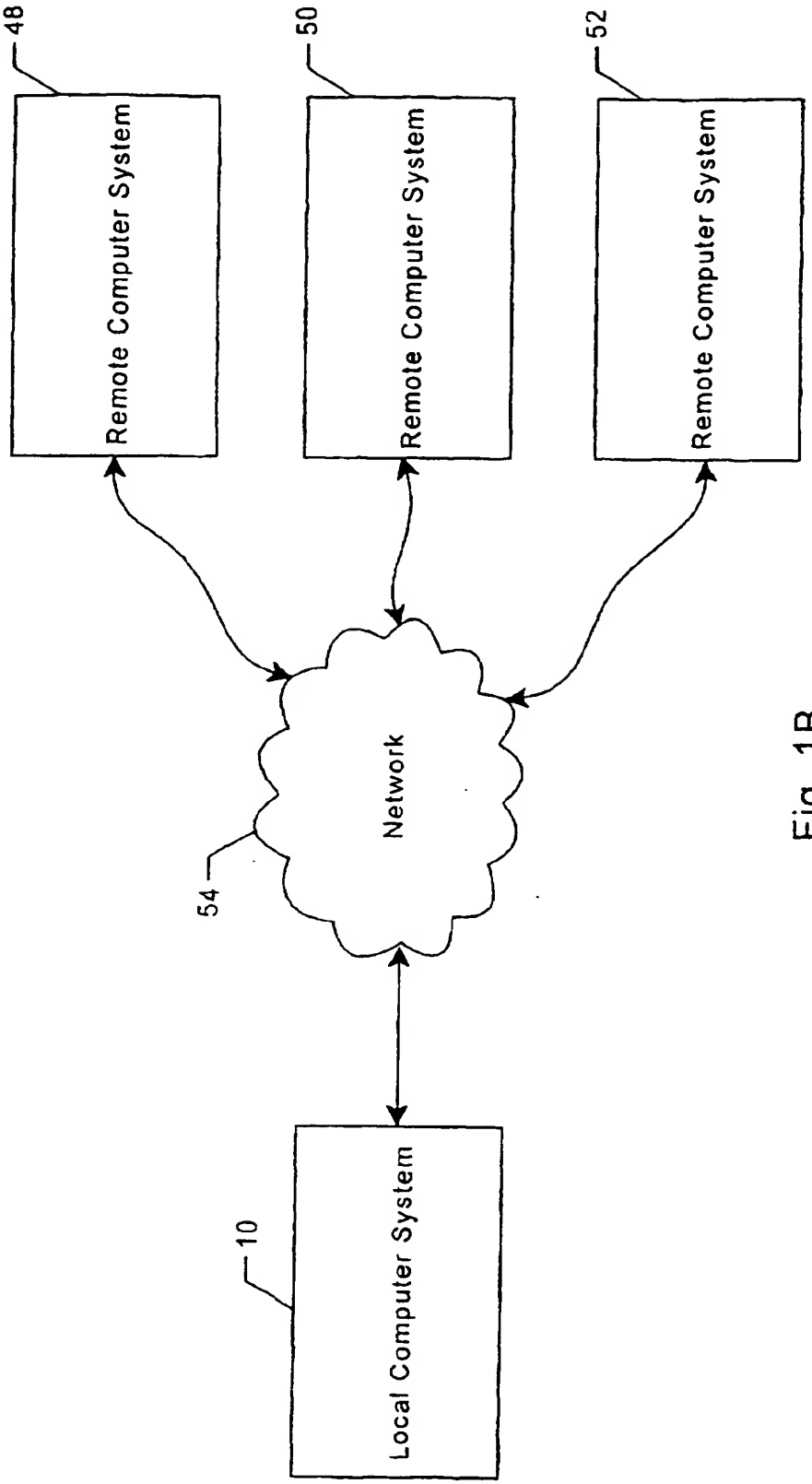


Fig. 1B

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(54) Polymorphisms associated with hypertension

(57) The invention discloses a collection of polymorphic sites in genes know or suspected to have a role in hypertension. The invention provides nucleic acids including such polymorphic sites. The nucleic acids can be used as probes or primers or for expressing variant proteins. The invention also provide methods of analyzing the polymorphic forms occupying the polymorphic sites.

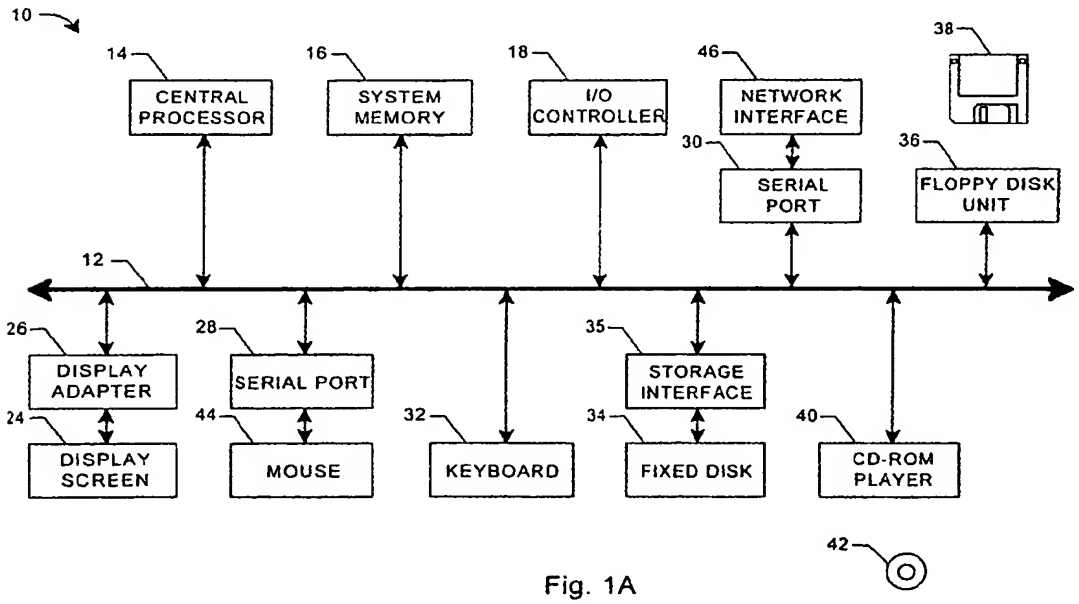

Fig. 1A

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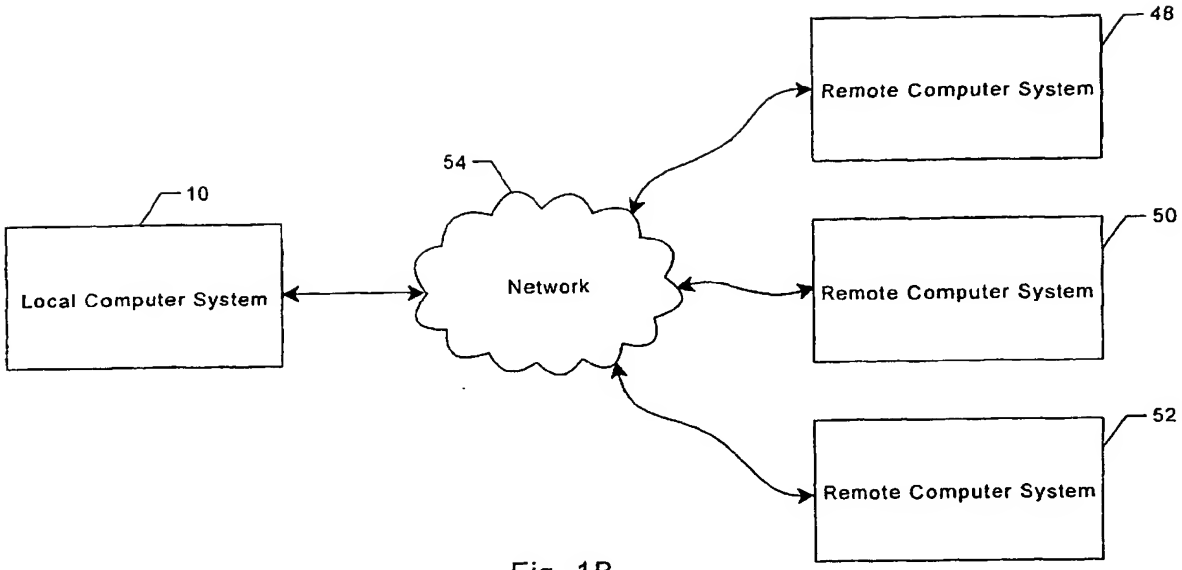

Fig. 1B

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EUROPEAN SEARCH REPORT

Application Number
EP 99 25 0150

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
X	WO 94 21790 A (UNIV BRITISH COLUMBIA) 29 September 1994 (1994-09-29) * see especially primer sequences ADU1524 and ADU133 within table 2 * * abstract; table 2 * ---	1,2,4,6, 9	C12Q1/68 C07K14/72 G06F17/30
Y	CUSI D ET AL.: "Polymorphisms of alpha-adducin and salt sensitivity in patients with essential hypertension" THE LANCET, vol. 349, 1997, pages 1353-1357, XP002127732 * the whole document * ---	21-32	
D,Y	JEUNEMAITRE X ET AL.: "Haplotypes of angiotensinogen in essential hypertension" AMERICAN JOURNAL OF HUMAN GENETICS, vol. 60, 1997, pages 1448-1460, XP000857377 * abstract * ---	21-32	
Y	WO 94 08048 A (INST NAT SANTE RECH MED ;UNIV UTAH RES FOUND (US)) 14 April 1994 (1994-04-14) * the whole document * ---	21-32	TECHNICAL FIELDS SEARCHED (Int.Cl.6) C12Q C07K
A	TAMAKI S ET AL.: "Polymorphism of alpha-adducin in japanese patients with essential hypertension" HYPERTENSION RESEARCH, vol. 21, 1998, pages 29-32, XP000862816 * the whole document * --- -/--		

~~The present search report has been drawn up for all claims~~

Place of search	Date of completion of the search	Examiner
THE HAGUE	14 January 2000	Knehr, M

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

European Patent Office

Application Number
EP 99 25 0150

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☒ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

1-9, 21-38 (partially), see invention 1.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 99 25 0150

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	BIANCHI G ET AL.: "Two point mutations within the adducin genes are involved in blood pressure variation" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA, vol. 91, 1994, pages 3999-4003, XP002127733 * see especially Fig. 1 * * the whole document * ---		
A	WO 88 08457 A (BIOTECH RES PARTNERS LTD) 3 November 1988 (1988-11-03) * the whole document * ---		
D,A	LIFTON R P: "Genetic determinants of human hypertension" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA, vol. 92, 1995, pages 8545-8551, XP002127734 * the whole document * ---		TECHNICAL FIELDS SEARCHED (Int.Cl.6)
T	HALUSKA M K ET AL.: "Patterns of single-nucleotide polymorphisms in candidate genes for blood-pressure homeostasis" NATURE GENETICS, vol. 22, 1999, pages 239-247, XP002127735 * the whole document * -----	1-9, 21-38	

~~The present search report has been drawn up for all claims~~

Place of search	Date of completion of the search	Examiner
THE HAGUE	14 January 2000	Knehr, M

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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European Patent Office

LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 99 25 0150

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-9,21-38 (partial)

INVENTION 1:
A nucleic acid from the gene encoding alpha-adducin including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

2. Claims: 1-9,21-38 (partial); 19,20 (complete)

INVENTION 2:
A nucleic acid from the gene encoding angiotensin converting enzyme including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

3. Claims: 1-9,21-38 (partial)

INVENTION 3 TO INVENTION 5:
A nucleic acid from the genes encoding beta-adducin, gamma-adducin, or A2a adenosine receptor, including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

Invention 3 refers to beta-adducin,
invention 4 refers to gamma-adducin, and
invention 5 refers to A2a adenosine receptor.

4. Claims: 1-9,21-38 (partial); 13 (complete)

INVENTION 6:
A nucleic acid from the gene encoding beta-3-adrenergic receptor including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a

European Patent Office

LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 99 25 0150

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

5. Claims: 1-9,21-38 (partial)

INVENTION 7 TO INVENTION 8:
A nucleic acid from the genes encoding (prepro)adrenomedullin, or anion exchanger, including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

Invention 7 refers to (prepro)adrenomedullin, and invention 8 refers to anion exchanger.

6. Claims: 1-9,21-38 (partial); 17 (complete)

INVENTION 9:
A nucleic acid from the gene encoding angiotensinogen including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

7. Claims: 1-9,21-38 (partial)

INVENTION 10:
A nucleic acid from the gene encoding aldose reductase including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

8. Claims: 1-9,21-38 (partial); 12 (complete)

INVENTION 11:

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LACK OF UNITY OF INVENTION SHEET B

Application Number
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The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

A nucleic acid from the gene encoding atrial natriuretic factor including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

9. Claims: 1-9,21-38 (partial)

INVENTION 12 TO INVENTION 19:
A nucleic acid from the genes encoding apolipoprotein A-I, apolipoprotein A-II, ..., apolipoprotein C-IV, or apolipoprotein E receptor 2, including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

Invention 12 refers to apolipoprotein A-I,
invention 13 refers to apolipoprotein A-II,
...
invention 18 refers to apolipoprotein C-IV, and
invention 19 refers to apolipoprotein E receptor 2.

10. Claims: 1-9,21-38 (partial); 11 (complete)

INVENTION 20:
A nucleic acid from the genes encoding angiotensin II receptor type-1 or angiotensin II receptor type-2 including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

11. Claims: 1-9,21-38 (partial)

INVENTION 21 TO INVENTION 23:
A nucleic acid from the genes encoding arginine vasopressin, arginine vasopressin receptor type II, or beta inward rectifier subunit (pancreatic K channel), including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide

European Patent Office

LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 99 25 0150

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

Invention 21 refers to arginine vasopressin,
invention 22 refers to arginine vasopressin receptor type II, and
invention 23 refers to beta inward rectifier subunit (pancreatic K channel).

12. Claims: 1-9,21-38 (partial); 14 (complete)

INVENTION 24:
A nucleic acid from the gene encoding B2 bradykinin receptor including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

13. Claims: 1-9,21-38 (partial)

INVENTION 25 TO INVENTION 64:
A nucleic acid from the genes encoding brain natriuretic protein, bombesin receptor subtype-3, ..., kallistatin, or kallikrein, including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

Invention 25 refers to brain natriuretic protein,
invention 26 refers to bombesin receptor subtype-3,
...
invention 63 refers to kallistatin, and
invention 64 refers to kallikrein.

14. Claims: 1-9,21-38 (partial); 15 (complete)

INVENTION 65:
A nucleic acid from the gene encoding mineralocorticoid receptor including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific

European Patent Office

LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 99 25 0150

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

15. Claims: 1-9,21-38 (partial); 18 (complete)

INVENTION 66:
A nucleic acid from the gene encoding sodium-calcium exchanger including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

16. Claims: 1-9,21-38 (partial)

INVENTION 67 TO INVENTION 75:
A nucleic acid from the genes encoding norepinephrine transporter, neuropeptide Y, ..., preprothyrotropin-releasing hormone, or prostaglandin E receptor EP3 subtype, including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

Invention 67 refers to norepinephrine transporter,
invention 68 refers to neuropeptide Y,
...
invention 74 refers to preprothyrotropin-releasing hormone, and
invention 75 refers to prostaglandin E receptor EP3 subtype.

17. Claims: 1-9,21-38 (partial); 16 (complete)

INVENTION 76:
A nucleic acid from the gene encoding renin including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal

European Patent Office

LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 99 25 0150

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

carrying data.

18. Claims: 1-9,21-38 (partial); 18 (complete)

INVENTION 77 TO INVENTION 81:
A nucleic acid from the genes encoding SA gene, amiloride-sensitive epithelial sodium channel gamma subunit, ..., thromboxane synthase, or thyrotropin-releasing hormone receptor, including a polymorphic site according to table 1, column 8, or the complement thereof, an allele-specific oligonucleotide hybridizing to such a polymorphic site, a method of analyzing such a nucleic acid, methods of diagnosing a phenotype related to such a polymorphic site, a computer-readable storage medium as well as a signal carrying data.

Invention 77 refers to SA gene,
invention 78 refers to amiloride-sensitive epithelial sodium channel gamma subunit,
...
invention 80 refers to thromboxane synthase, and
invention 81 refers to thyrotropin-releasing hormone receptor.

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 99 25 0150

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

14-01-2000

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82